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VESICAL TUMOURS INDUCED BY CHEMICAL COMPOUNDS

BY

M. W. GOLDBLATT

London

(RECEIVED FOR PUBLICATION, AUGUST 27, 1948)

The accumulated records of cases of vesical tumours occurring among workers in that part of the chemical industry which deals with organic intermediates, especially aromatic amines, would seem to be sufficient to justify the conclusion that there is such a thing as aromatic amine cancer. The impressive figures of Gehrmann (1936) in the United States, Müller (1933) in Switzerland and di Maio (1937) in Italy, apart from the German data, amply confirm the statement of di Maio " che i tumori e le lesioni precancerose della vescica negli operai delle fabbriche di nitro derivati sono frequentissimi," although one would wish to substitute amines for nitro derivatives. di Maio's figures are especially striking: he found between 1931 and 1937, among eighty-six workers in two factories engaged in manufacture of aromatic amines and nitro compounds, four bladder cancers, seven papillomata, and twenty-six cases of a variety of vascular lesions (simple congestions, varicosities, and telangiectasis) which he regarded as precancerous. di Maio's figures were collected by the only method which at any given time can give a true incidence of the disease in any group, viz., by cystoscopic examination of the whole group.

J. C. Bridge, who was, to the end of his life, most active in his attempts to eradicate the disease from the chemical industry and to establish an equitable basis for compensation of this, in Britain, non-scheduled industrial disease, published some striking figures in his 1933 Report to the Chief Inspector of Factories. These figures showed that in one of the smaller manufacturing towns in England where the manufacture of organic intermediates had been going on for many years, the admission to the local Infirmary of cases of bladder tumour were as follows:

1900–1910.	12	males	of	whom	3	were	chemical	labourers
1911–1921.	15	,,	,,	,,	3	,,	,,	,,
1922–1932.	37	,,	,,	,,	26	,,	,,	,,

Between 1929 and 1932 the admissions were:

1929.	5	males	of	whom	4	were	chemical	labourers
1930.	4	,,	,,	,,	4	,,	,,	,,
1931.	10	,,	,,	,,	9	,,	,,	,,
1932.	4	,,	,,	,,	3	,,	,,	,,

Examination of these figures shows that this Infirmary was, excluding the chemical labourers, getting an average of about one case a year and that the presence of the relatively very few chemical labourers just doubled the average for the thirty-two-years period. In addition, it was reported that for the period 1928–32 the estimated mortality rates for this disease among chemical workers was thirty-eight times higher than for the male insured population of the town.

Having regard to the fact that in Britain, routine cystoscopy is not practised in the relevant chemical factories and that during the greater part of the period reported on by Bridge no routine urine examinations were carried out and, further, that the condition is symptomless in the early stages, and finally that there is a considerable labour turn-over in factories of this kind, we may be tolerably certain that the actual incidence of bladder tumours was at any given time higher than that recorded.

It is not our intention to review the literature on this subject but mention must be made of a recent addition to it. It has been something of a puzzle for some time that cases of vesical tumour arising in the chemical industry had not been significantly reported in France in spite of a considerable organic chemical industry. It is therefore, of interest and importance that Billiard-Duchesne should have very recently published (1947, 1948) an account of seventeen cases collected during recent years. The author calculated that in the factory concerned the proportion of vesical tumours among the workers was forty-three times that in the general population. In this series of cases the youngest was 39 years of age and the oldest 74 years: the mean was 53 years,

and the author concludes that, this also being in the region of so-called spontaneous cancer, age of onset is really a "facteur second, consécutif." This is a dangerous conclusion and, without more detailed data and analysis, cannot be accepted, for the age of onset depends on the age of entry into the industry, as will be shown.

Billiard-Duchesne, like all other students of this condition, relates the disease to inhalation and absorption *per cutem* of the napththylamines and benzidine. Accepting five years as the minimum period of exposure necessary to induce a vesical tumour, he thinks it reasonable to recommend that no worker should be maintained in the hazardous operations for more than this period. He further considers that the French Law of Dec. 9, 1938, Art. 15, which extends to intoxications caused by aromatic amines the provision of the law of April 9, 1898 (Accidents at Work) and which would limit the period of responsibility for compensation of cases of bladder tumours to five years after leaving the injurious work, should be amended to entitle to compensation up to at least ten years after cessation of employment in the hazardous processes. Doubtless these matters will be argued in France as they have been elsewhere, and one can but hope that the well-known perspicacity of our French colleagues will succeed where as yet no finality has been reached elsewhere.

Billiard-Duchesne supports routine cystoscopy as the major method for the detection of what he rightly calls "tumeurs silencieuses" of the bladder, and states that refusal to undergo this procedure is not as frequent among workers duly informed of the hazard of their work as it is among those who, believing themselves well, recoil from an allegedly disagreeable examination.

Another paper has been recently published in France by Désoille and others (1948). They found that, of two hundred workers in a dye factory who had worked in it for more than five years, twenty-eight showed a positive qualitative test for blood in urine. Twenty-five of these agreed to be cystoscoped and twenty-three were actually cystoscoped. Of these twenty-three men, five showed bladder tumours and five showed bladder abnormalities. Four of the tumour cases had worked for many years in naphthylamines and one had worked for eighteen years in mercaptobenzthiazol (this latter, provided the worker had no other carcinogenic exposure, would be reckoned as an aniline case, since this is the only amine used in this synthesis). The five cases with bladder abnormalities showed vascular dilation, telangectases, and sub-mucous ecchymoses, changes which may be regarded as pre-neoplastic.

As a result of thus discovering 5 per cent. of the men with tumours or pre-tumour changes the investigation was "interrompue par suite du départ forcé, par la direction de l'usine, de l'un de nous," a terrible comment even in this epoch of savagery.

The attitude of workers in Britain toward cystoscopy is far from favourable. Having had an opportunity of seeing di Maio performing routine cystoscopy in an Italian factory, I can affirm that, given the right state of mind in the workers, no difficulty need be anticipated. It would appear that American and Swiss experience is similar.

There was recently an opportunity of examining the record of cases of bladder tumours in the I.G. organization in Germany; it was found that in Professor Gross's files at Elberfeld there were records of between 300 and 350 cases.

Interviews in factories of this organization elicited some interesting data.

FACTORY LE

Period	No. of workers	No. of cases	Significant chemical compound	No. of deaths
1920–1938	500	21	Aniline, Benzidine	?
	40–45	20	β-naphthylamine	15
	?	5	?	?

One case, specially noteworthy, was that of a worker in benzidine who developed a bladder tumour after only six months' exposure.

It was stated by medical and chemical officials that no cases had occurred among workers engaged in the manufacture and use of α-naphthylamine (containing up to 5 per cent. β-isomer).

FACTORY LU

Extract from paper by Gross (1940)

Total period since establishment of the factory	60 years
Total number of bladder cancer cases	85
Aniline	33
β-naphthylamine	36
Aniline + β-naphthylamine	13
Benzidine base	3
Shortest period of exposure	6 months
Latent period between cessation of exposure and onset of disease	34 years—maximum
	25 years—minimum
Age at onset of disease	50–55 years
Age of highest incidence	
Proportion of workers in β-naphthylamine for over 5 years who developed bladder tumours	33%

Gross stated that the age-mortality frequency curves of workers with cancer of the bladder compared with that of the general population in the neighbourhood of the works, shows that the

shortening of life is only by a few years. It is admitted that large numbers of exposed workers could not be traced.

It will be noted that in Factory Le nearly 50 per cent. of the men in β-naphthylamine developed tumours of the bladder and something like 37 per cent. were already dead from the disease in 1938.

Analysis of Cases of Vesical Tumours Detected in Two Factories During the Period 1934 to 1947

Nature of the Factories

The factories were large chemical factories engaged in the manufacture of a wide variety of organic intermediates and dyestuffs, rubber chemicals, textile finishing agents, organic primaries, and many other compounds.

The smaller of the two factories dates back to the last quarter of the nineteenth century, the larger to the twenties of the present century. Both have undergone great development both in magnitude of production and modernization of plant and process. In both, increasing awareness of the hazards has led to notable advances in measures designed to diminish the evolution of toxic fume and dust, to diminish skin contact with the products, and to improve the physical amenities for the workers.

Medical services have been extended and a variety of procedures introduced to determine the concentration of toxic amines in the working environment, to determine the excretion of amines by the workers, to promote diuresis in the workers, and to detect the onset at the earliest stage of exfoliation of the bladder epithelium and hæmaturia by routine microscopic examination of the urine. The effective removal of certain amines from the skin by ablution is tested by ultra-violet fluorescence, where the relevant substance gives a marked fluorescence, for example, β-naphthylamine.

Routine cystoscopy is not practised. Cystoscopy is recommended by the medical officers at such times as the condition of the urine and the history of the case appear to justify it. It is fully realized that this method of control offers no certainty that tumours will not be missed in the earliest stages. Until the attitude towards routine cystoscopy is changed and the urological technique is such as not to raise both painful memories in the experienced and anxious apprehension in the neophytes, we shall be compelled to continue the present practice, imperfect as it is.

The potential of cases built up in these factories will only be discharged in a great many years to come. The burden of study at present is to devise methods of manufacture and design of plant which will eliminate the hazard.

Nature of Processes

The processes were a mixture of classical methods and others based on invention and experience. In the manufacture of the amines of interest in the present connexion the methods were for aniline the classical acid reduction of nitrobenzene, for α-naphthylamine the Fe-HCl reduction of α-nitro-naphthylamine, for β-naphthylamine the ammonium sulphite-ammonia amidation of β-naphthol, and for benzidine the electrolytic reduction of nitrobenzene in alkaline conditions and in the presence of a suitable solvent to dissolve the hydrazo-benzene which is subsequently separated from the solvent and subjected to the usual acid treatment for conversion to benzidine hydrochloride.

The subsequent working up of these aromatic amines is so extensive and technically complex that it must suffice here to state that hundreds of different products are produced which involve greater or less processing of the amines, for example, sulphonations, nitrations, chlorinations, diazotization, alkylation, arylation, condensations with aliphatic aldehydes, hydroxylation, formation of nitroso compounds, and many others.

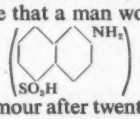
It is certain that, in spite of many precautions and improvements introduced in recent years, the workers do come into significant contact with a great variety of compounds among which the supposed bladder carcinogens must be included. It would be deluding oneself to suppose that more than the first move in complete enclosure of processes has been attained. Study of plant in Germany, Switzerland, and Italy has shown that each has made some contribution to safe working principles but all have a long way still to go.

Do what we may, there are operations in this industry which inevitably expose men to dust and sometimes fumes, for example, flaking, drying, grinding, filtering. Shovelling toxic products into reaction vessels is notorious as a dust disseminator. By the expenditure of a little thought and money it is possible, for many products, to eliminate shovelling altogether by fitting a suitable adaptor to standard drums, raising the drums by suitable tackle, and tipping in the charge through the adaptor into the reactor.

With free flowing solids this can be done with ease. With a product which contains a proportion of an isomer with which a eutectic mixture easily forms, difficulties may be met with in obtaining free flow.

The German method, a good many years ago introduced into one of the factories referred to above, whereby molten α-naphthylamine is pumped through steam-jacketed pipes to the sulphonators for production of naphthionic acid, is highly effective.

Flaking of naphthylamines is a vastly more satisfactory procedure than solidification of condensates and subsequent breaking up and grinding. But even a good flaking machine can be a potential source of dust and fragments of amine. Whilst the chamber under the flaker in which the drums are filled through a hood can be draughted and kept very clean, the dust and débris most often seen round a well-run flaker emerges from the collecting and "doctoring" chamber.

Whatever precautions may be taken, somewhere or other a product must emerge from the plant and this point of emergence is a potent source of trouble. Ideally the toxic amine should be manufactured at a central point and distributed mechanically to peripheral plants where the subsequent stages in building up the intermediates can be carried out. In practice, this is rarely possible. Were this possible a high proportion of men would thereby be released from the need to handle, for example, β-naphthylamine. Thus, Billiard-Duchesne reports his surprise that a man working in the manufacture of γ-acid  developed a malignant bladder tumour after twenty-three years of shovelling β-naphthylamine into the autoclave containing the sulphonating mixture. Had the amine been transferred to the autoclaves in the manner suggested above, this man might have escaped altogether.

Since nitro compounds are ubiquitous in the industry it is important to state that we have no evidence of carcinogenic properties in any of them. In a factory in which we have run control observations for many years and in which nitro-benzene is an almost universally used reaction medium and in which a great variety of aromatic nitro and amino bodies are used and made, no single case of bladder tumour has been discovered.

Similarly, we have no reason to suspect sulphonic acids.

Most observers will probably agree with these conclusions. Arising from this it may be mentioned that efforts are being made in Britain and in Switzerland and were made, we were informed, in Germany, to avoid the isolation of β-naphthylamine base by sulphonating β-naphthol to oxy-Tobias acid and subsequent amidation to Tobias acid. Higher sulphonation products from this acid can readily be prepared. Tobias acid itself is used as a first component in many azo dyes.

Some β-naphthylamine base will, however, still be required as such for certain products but the hazard will be greatly diminished if the Tobias acid synthesis is made practicable on a large scale.

Except in one concern in the U.S.A., α-naphthylamine is still, as far as we know, manufactured by the classical method indicated above. If the reduction by Fe-HCl is replaced by catalytic hydrogenation we do not remove the proportion of β-naphthylamine which is held by many investigators to be the real carcinogenic agent but we do remove the hazard of the reduction process itself. If, further, the base is distilled, transported to the point of further working up in heated tank wagons and drawn into reactors by specially adapted suction or pressure appliances with automatic devices to prevent the issue of fume, the hazard can be still more reduced.

Benzidine offers many difficult problems if any process other than the classical Zn-NaOH reduction is used. Yet in a factory in Italy this process was operated in the most primitive conditions and we had the assurance that no bladder tumours had been discovered. The truth of this statement probably depended on the facts that (*a*) hydrazobenzene was not separated and (*b*) the conversion was carried out by direct transfer of a neutralized slurry to the conversion vat, addition of HCl, and later precipitation of the sulphate. At no stage was it necessary for the process worker to handle hydrazobenzene or benzidine base or hydrochloride. The highly insoluble sulphate was filtered on a press and stacked in the yard.

It seems reasonable to regard benzidine sulphate as innocuous but from the industrial point of view there are objections to it. The mono- and di-hydrochlorides are preferred in this country. Basification has been forbidden in the factories under my supervision for some ten years or more.

Whereas α- and β-naphthylamine from the nature of the flaking process inevitably emerge in a dry dusty form, benzidine hydrochloride can be maintained moist and no drying of this product has been permitted for ten years at least.

With a compound like aniline which can produce fulminating acute symptoms it is not surprising that the technique of manufacture and use should have reached higher standards of safety than in the case of the other more subtly acting toxic amines. Cyanosis due to aniline is, in a modern factory, relatively uncommon in the normal working of processes; it is common as arising from solid amines, nitro-amines, chlor-nitro-amines, and the like, which penetrate the skin and are inhaled as dust. Solids are never as impressive to a worker as toxic agents as are liquids and above all, gases.

The question of aniline as a carcinogenic agent has passed through the early phase when it was regarded as the type amino carcinogen to the present phase when it is almost entirely exonerated. It would be unwise to be over dogmatic either way.

In the data we will present it will be at least clear that we, in this country, must take an open view.

Certain azo compounds having been shown experimentally to be carcinogenic, it is natural to wonder whether such compounds may not be significant in our problem. It would require a rash man to answer this question with a categorical negative. Such an answer would at least be comforting to all of us having regard to the nature of some of the æsthetic shades with which we beautify our foods. The metabolism of azo compounds in the body is still a subject requiring much more investigation. Cases of bladder tumour arising in an azo department of a chemical factory are, in general, explicable by the nature of the primary amines or diamines which are handled. Were azo compounds, as such, very significant carcinogens, we should have expected a very high incidence among workers engaged for many years in the grinding and mixing of a great variety of simple and complex azo dyes. This is not, however, the case, and hence for the time being we are not in a position to be even approximately certain about azo compounds. The experimental results obtained with, for example, o-amino azo toluene, p-dimethyl-amino azo benzene, and scarlet red (diazotized o-amino azo toluene coupled with β-naphthol) provide knowledge which should lead to improved handling of such compounds, *but* it is not possible for us as yet to assess the weight of responsibility which compounds of this kind bear in the ætiology of bladder tumours as they occur in factories.

In condensing thus briefly some of the points in processes which appear significant in the problem of bladder tumours one cannot omit to draw attention to the manifold activities in the industry which may be called ancillary to manufacture and which lay men open to the dangers of carcinogenic agents. We will present data on workers who, whilst never employed in process work, yet developed bladder tumours. This is a matter of great moment in any attempted formulation of a scheme of legal compensation, for to restrict compensation only to men engaged on prescribed processes in a factory manufacturing organic intermediates would be highly unjust.

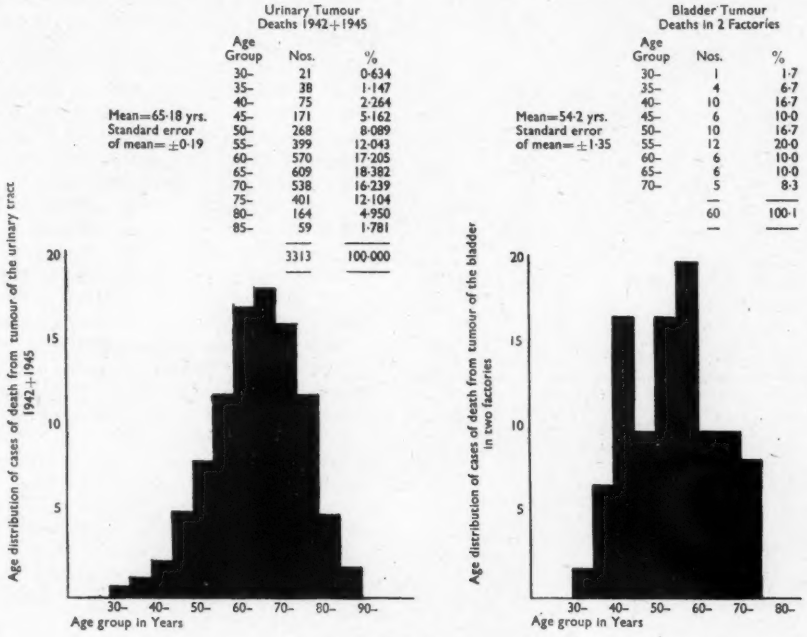


FIG. 1

ANALYSIS OF CASES

In the data now to be presented the cases from the two factories referred to have been considered together. All the patients (except one) were men who belonged to the same social stratum, worked

and lived in adjacent counties, and consumed similar diets, and they are not likely to have differed much in intellect or habit.

TABLE 1

ANNUAL INCIDENCE OF NEWLY ARISING VESICAL TUMOURS AND OF DEATHS FROM VESICAL TUMOURS IN TWO FACTORIES IN BRITAIN*

Year	Total No. workers in 2 factories	No. of tumour cases coming to light	per 10^4	Deaths from tumour	per 10^4
1934	2,025	7	3,456	1	493
1935	2,379	6	2,522	2	840
1936	2,414	8	3,315	1	414
1937	2,555	3	1,174	1	391
1938	2,225	12	5,392	7	3,146
1939	2,815	8	2,842	3	1,065
1940	3,183	4	1,257	5	1,571
1941	3,066	7	2,283	3	978
1942	2,952	4	1,355	6	2,033
1943	2,723	9	3,305	5	1,836
1944	2,808	6	2,137	6	2,137
1945	2,939	12	4,083	8	2,722
1946	3,863	7	1,811	6	1,554
1947	4,163	6	1,441	5	1,201
		99		59†	
Averages per year		7		4·2	

* The Table records cases from ages 30— to 70—, and cases were sometimes reported from retirement. Retired cases were reported in respect of possible *ex gratia* compensation. There is little doubt that the total incidence is higher, since some cases are missed through the men leaving the districts and doctors not knowing about the industrial aspects of the disease.

† The disparity between 59 in the Table and 60 in fig. 1 is due to the absence of the necessary data other than age in one case.

Comparisons between data of this kind and national figures are subject to certain difficulties. First of all we have no published national record of morbidity: secondly, we have no published national records of death due to bladder tumours but only of deaths due to all tumours of the urinary tract: thirdly, the age distribution of a fluctuating population such as we normally find in a large factory is difficult to correct for: fourthly, the social stratum from which the workers in the two chemical factories are drawn is that with which higher incidences of neoplastic disease is associated: fifthly, we do not know the numbers of men engaged in the particular branch of the chemical industry throughout the country nor the annual incidence of bladder tumours among them. Hence, although the incidence of deaths shown in Table 1 far exceeds the incidence of deaths for *all urinary tumours* in the country (1,623 out of a male population of 16,802,000 in 1942 and 1,758 out of a male population of 16,412,000 in 1945) it is perhaps more reasonable to compare with a similar population drawn from the same social stratum, employed on similar work but not using or making certain compounds and subject to a labour turnover of a similar kind. Since the two factories are associated with a group of factories spread over the country and engaged in different stages of the manufacture of dyes, pigments, and paints, but not in the production of primary aromatic amines (although these were used), and since the total number of workers in the group is about equal to that of the two factories, and since, further, the reported incidence of bladder tumours in the group is quite negligible and of deaths due to bladder tumours has been zero during the last thirteen years, it seems not unreasonable to associate the disease in the two factories with the manufacture of the amines. The expected incidence of *deaths* due to urinary tumours as a whole in a representative sample of the male population between the ages of 20 and 65 in England and Wales is less than 1 in 10,000, probably more nearly 1 in 20,000 for bladder tumours, so that an average incidence of 4·2 deaths per annum for a group of 2,000 to 3,000 men requires little comment.* Perhaps even more impressive is the consistency of the incidence of both newly appearing tumours and deaths.

If now, we proceed to consider the age distribution of these deaths it becomes apparent that the disease is one attacking its victims at ages much lower than those found among the general population.

Whereas some 4 per cent. of deaths due to urinary tumours in England and Wales at ages over 30 occur at ages less than 45 (1942 and 1945), in our industrial bladder tumour cases over 25 per cent. fall within the same age limit. This important difference is shown graphically in fig. 1, and depends upon the age at which the worker enters the industry. This is shown in fig. 2.

The implication of this is not that young men are more susceptible to the disease than are older men; on this we have found no data and, even if we had, rigid conclusions would have been dangerous in view of the impossibility of assessing the intensity of exposure to the hazards. The implication is simply that young men if they later develop a tumour and die from it, will in a great proportion of cases, die young. The same thing can be inferred from the mean time between entry into the industry and the onset of a tumour (nineteen years with a standard error of only 0·8) having regard to the

* By "representative sample" is meant the sample represented by the males living in a given year. Thus:

	Males	Urinary tumour deaths between ages 20 and 65	Deaths per 10^4
1942	16,802,000	1040	0·62
1943	16,412,000	1118	0·68

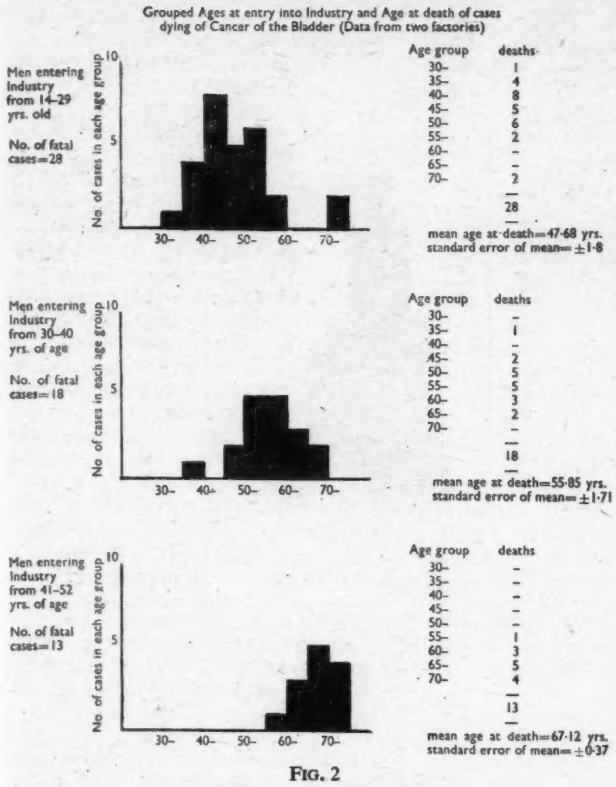


FIG. 2

high mortality (*vide infra*). But an implication that must be faced is that young men should not enter the industry so long as there is reason to believe the hazard of bladder tumour continues and if it is held that one of the objects of industry is, as far as possible, to assure all employees a reasonable length of working life. This course is not proposed as a substitute for making the dangerous processes safe. It is proposed because it is an extremely difficult matter to make them safe and because young inexperienced men are more likely to take risks and less likely to believe that they can sustain a serious damage from apparently innocuous substances.

This view on the employment of young men is contrary to that of well-known authorities on this problem and, until such time as the hazard is overcome, we will continue to maintain it.

In fig. 3 we present the frequency in 93* cases of different age groups at which tumours were first recognized. It is seen that 33 per cent. of the cases were diagnosed before the age of 45. When it is remembered that the method of detection of the onset of the growth was routine urine examination and not routine cystoscopy, it will be clear that the mean age of onset is less than the 50·55 given in the Table. As already stated above, the real determinant of the age of onset is the age at which the industry is entered.† We are not in a position to assess such factors as constitutional disposition to cancer. It may be that a family history of neoplastic disease is a significant factor. It is the fashion to prescribe that persons with a family history of neoplastic disease should not be employed in the industry. It may be that some industrial medical officers can elicit an informative family history from workers; most will probably agree that this is no easy matter. It is stated that not all workers in the hazardous processes develop bladder tumours. Hueper (1946) states that from 30 per cent. to 90 per cent. of workers in these processes develop tumours. We have recorded reminiscences of works chemists who had worked in some of these processes for many years and who stated that substantially every man they had had in the plant years before had since died of cancer of the bladder. The importance of maintained exposure to the hazardous compounds is indicated by the rarity of bladder tumours among chemists who have been in charge of the processes for many years. In our series of 102 cases up to date, only one chemist appears as having developed a bladder tumour and his works history indicated a much greater contact with the compounds than is nowadays usual for chemists in manufacturing plant. He was engaged for many years in the actual manufacture of many diamines, including benzidine, in a small factory since closed down: other contacts were α-naphthylamine and aniline.

When tabulations are made of the periods elapsing between first entry into the industry and

* In only 93 cases was the necessary information available.

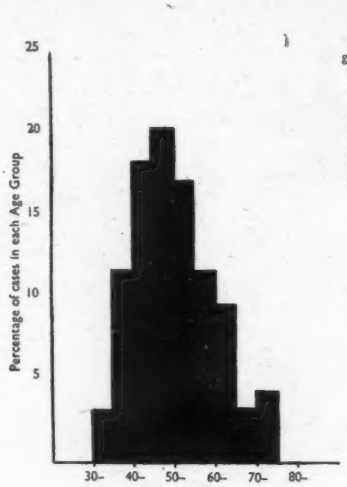
† There is no constancy of the period between age of onset and age of entry, for different age groups; for example, a man entered the industry as a boy of 14 years of age and developed a tumour at 70 years of age. Clearly the determining factor (mentioned elsewhere in the paper) is the degree of exposure over years, which is not measurable, and some perhaps constitutional predisposition. More research will be needed on this question.

the first discovered signs of tumour formation, emphasis is usually laid upon the minimum period at which a tumour may be found. In fig. 4 a distribution of periods elapsing is given for 100 cases in our series which yields a mean of some nineteen years (standard error 0·8).

These cases may, of course, have developed the tumour whilst in the industry or many years after having left it. Thus, as a typical example, we have the case of S.H.H. who worked in β-naphthylamine for three and a half years, left the industry, and died of carcinoma of the bladder twelve years later at the age of 57 years.

Another case of interest was a man who had worked in the industry for one year, and three months from *the time of starting* was found to have a small sessile papilloma above the left ureteric orifice. In spite of statements that six months' exposure may be sufficient to lead to tumour formation (Koelsch, 1935), this case was recorded as non-occupational. The single case in fig. 4 developing a tumour in less than six years was a fitter who for *two years* was engaged in the maintenance of β-naphthylamine autoclaves: he had no further contact, and two years later developed a bladder papilloma, that is, four years after entering the industry. This was the shortest period of exposure and the shortest latent period in the present series. This man had a recurrence twenty months after the first tumour was fulgurated and now, nine years afterwards, is apparently quite well.

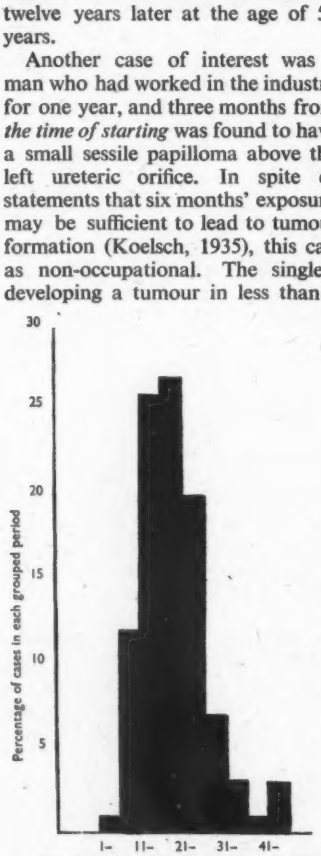
Ages at first recognition of tumours (living and dead cases) where known. Data from two factories



Age group	First recognition of tumour Nos.	%
30–	3	3·23
35–	11	11·82
40–	17	18·28
45–	19	20·43
50–	16	17·20
55–	11	11·82
60–	9	9·68
65–	3	3·23
70–	4	4·30
	93	99·90

Mean = 50·55
σ = 9·85
Standard error of mean = ±1·1

FIG. 3


Percentage of cases in each grouped period
30
25
20
15
10
5
1- 11- 21- 31- 41-
Period of years from first entry into Industry till first discovered tumour (living and dead cases). Data from two factories.

Period In yrs.	Nos.	%
1–	1	1·0
6–	12	12·0
11–	26	26·0
16–	27	27·0
21–	20	20·0
26–	7	7·0
31–	3	3·0
36–	1	1·0
41–	3	3·0
	100	100·0

Mean = 18·95 yrs.
σ = 8·0
Standard error of mean = ±0·8

FIG. 4

The root problem in the pathology of the disease lies in this Table, for what must ultimately be determined is the nature of the change in the bladder (mucous membrane or connective tissue) which can manifest itself as a tumour many years after cessation of exposure.

Some experimental work in the U.S.A. (referred to privately by Dr. Gehrmann) appears to have shown that β-naphthylamine can be demonstrated in the bladder tissue of animals years after the last dose had been administered. If this were confirmed it would not remove the dilemma of imagining a carcinogen quiescently in contact with a tissue for, in some cases, forty years. Perhaps it could be more easily imagined if, as was suggested in a former paper (Goldblatt, 1947), the amine were a potentiator of the tissue which must await

the adequate concentration of endogenous carcinogen to develop a tumour. Production of tumours in animals could, on this view, be regarded as resulting from an enormous amount of potentiator to produce the necessary and sufficient conditions for a very small available amount of carcinogen to be effective to produce a tumour.

The pre-cancerous vascular changes which are seen in the bladder might be regarded as the signs of the action of the potentiator. There is no doubt that exfoliation of bladder epithelium, intermittent microscopic hæmaturia, and leucocytes in the urine can proceed for months and even years without any overt tumour being detectable cystoscopically.

The occupational variety of bladder tumour is almost always preceded by one or other or all of these signs. It is true that a tumour may occasionally be present without hæmaturia being detectable, but more or less bladder epithelium is always to be found in the urine of these cases.

But it is not so easy to picture what is occurring when at the time of leaving the industry no signs whatever can be detected in the urine and yet a tumour develops after a few or many years without any further industrial exposure. Parallel problems are, of course, to be found in various kinds of occupational neoplastic disease.

The nature of the substance or substances which are responsible for setting in train the process of tumour development in the bladder is not yet known with certainty. Whereas β-naphthylamine has been shown experimentally to be a carcinogen in dogs, it must be allowed that the doses used to produce tumours have been enormous. In Table 2 we set out some data to give an idea of the order of excretion of aromatic amine among workers engaged in the manufacture of α-naphthylamine in conditions at first bad and later much improved. Since the determinations were carried out on "grab" samples, an assumption had to be made of the total daily volume of urine. The volume assumed was 1,500 ml. The numbers of samples tested were 119 in 1942, 100 in 1943, and 100 in 1944.

Conditions in these plants were progressively improved with resulting great diminution in excreted amine but, even at the worst period, average excretion did not exceed 1–2 mg. per kg. body weight per day (assuming average body weight to be about 70 kg.) and was reached at only two spots in 1942. This is shown also in Table 3. Here we see that in 1942, 21 per cent. of the samples, in 1943 only 7 per cent., and in 1944 only 6 per cent. exceeded 61 mg.

If we take these figures as some indication of the degree of absorption of amine, it is at once seen how the dosage of dogs by, for example, Bonser (1943) exceeds the absorption found in practice. This investigator started her dogs on 150 mg. per

TABLE 2

AVERAGE DAILY EXCRETION OF AROMATIC AMINE PER WORKER PER 1,500 ML. URINE (AS MG. α-NAPHTHYLAMINE)

	1942	1943	1944	
Plant :				
Primaries Section	39·5	12·9	8·0	Section in which a variety of amines and other primary products are handled
α-naphthylamine plant ..	41·7	20·0	12·3	Figures for individual parts of the plant —below
α-nitronaphthalene plant ..	3·0	3·0	2·8	—
Naphthionic acid and sodium naphthionate ..	81·0	8·2	7·4	—
Foremen	1·3	1·0	0·7	—
Individual parts of α-naphthylamine plant :				
Reduction	53·4	14·8	6·1	—
Distillation	24·0	13·3	10·9	—
Flaking	74·8	69·5	43·6	Note maintained high excretion here in spite of improvements.
Miscellaneous jobs	33·8	8·8	4·3	—
Total for whole plant ..	41·7	20·0	12·3	—

day of β-naphthylamine, and changed over to 100 mg. per day because of hæmaturia; but after the first year of treatment the dose was gradually raised to 700 mg. per day.

TABLE 3

DISTRIBUTION OF AMINE CONTENT OF WORKERS' URINE; PERCENTAGE OF SAMPLES ANALYSED

Amine, mg.	1942	1943	1944
<2·0 ..	5·9	35·0	61·0
2—	42·9	50·0	24·0
21—	30·2	18·0	9·0
61—	15·1	3·0	4·0
120—	5·9	4·0	2·0
No. of samples ..	119	100	100

Now when it is remembered (1) that it is in conditions such as the above that tumours develop, and (2) that the α-naphthylamine produced in this plant contains only 3 per cent. or 5 per cent. of β-naphthylamine, then the doses given by Bonser seem fantastically large in relation to what is needed for a man (if we accept the widely held view that α-naphthylamine as such is not tumour-producing).

Whilst Bonser's experiments leave no doubt that β-naphthylamine can lead to bladder tumours in dogs, it is desirable to simulate the human situation by giving doses which are entirely undisturbing.

Experimental evidence that primary aromatic amines other than β-naphthylamine are tumour-producing has not as yet been published, as far as we know. Evidence from the nature of the exposure of affected workers is difficult to elicit, for, from the nature of the industry, maintenance of workers on single processes is not, in general, possible. The matter is made still more difficult by bladder tumours appearing in men who were not officially attached to any of the suspected processes.

In our series of cases it has been possible to pick out men who were, owing to special circumstances, attached exclusively to one process. Thus, the α-naphthylamine process was carried out in an old plant which had been modernized in many important respects (although still unsatisfactory), and there were men who had been associated with it exclusively for many years. In the case of β-naphthylamine the process had gone through some vicissitudes since up to some ten years ago it had been one of several processes which stood in a single large shed (and had affected a number of men who officially had nothing to do with the process itself) and since that time has stood on a separate site and has become more or less an open-air process. This process and those for aniline and benzidine are located in another town some thirty miles away from that for α-naphthylamine.

Men who had been associated only with the manufacture of aniline, benzidine, or β-naphthylamine were picked out. Such men are by no means the only ones to have been in contact with these products.

It has thus been possible to construct tables of fifty-eight cases of bladder tumours among men with different known times and nature of exposures and of eighteen cases among men the nature of whose exposures were known but the times unknown (Tables 4 and 5). Of these fifty-eight cases, 26 were of papillomata at the start and thirty-two were of carcinomata at the start.

It will be observed that the proportion of cases in Table 4 starting as carcinoma is greatest where β-naphthylamine has been the only chemical suspect or one of the chemical suspects. In only one of these cases was a papilloma diagnosed: in one diagnosis was doubtful (Table 5).

It will be noticed also that in all but two cases of these groups of cases β-naphthylamine was manufactured or handled.

TABLE 4

NATURE OF FIRST TUMOURS: PERIOD AND NATURE OF CHEMICAL EXPOSURE

(Only those cases are included in which periods in specific substances are known with some accuracy)

Period in various substances (yrs.)	Aniline only		α-naphthylamine only		β-naphthylamine only		Benzidine only		Mixed exposure including all the preceding	
	P	C	P	C	P	C	P	C	P	C
1—	—	—	1	—	3	2	—	1	—	3
6—	—	—	—	—	3	8	—	—	1	4
11—	1	—	3	1	1	2	1	1	2	2
16—	—	—	1	—	2	1	2	1	—	2
21—	1	—	3	1	—	—	—	—	—	2
26—	1	—	—	1	—	—	—	—	—	—
	3	0	8	3	9	13	3	3	3	13

P = papilloma. C = carcinoma.

TABLE 5

NATURE OF FIRST TUMOUR OR TUMOURS IN MEN WHOSE PERIODS OF WORK IN VARIOUS PROCESSES ARE NOT KNOWN

No. of cases (18)	Nature of tumours	Aniline	α-naphth.	β-naphth.	Benzidine
2	C	+	+	+	+
2	C	+	−	+	+
4	3 C ; 1 ?	+	−	+	−
3	C	−	−	+	+
4	3 C, 1 P	+	+	+	−
1	C	+	+	−	−
1	C	−	+	+	−
1	C	+	+	−	+

P = papilloma. C = carcinoma.

If aniline and α-naphthylamine, benzidine and β-naphthylamine, and mixed exposures are regarded as three groups giving increasing proportions of carcinoma (Table 4), it is perhaps just permissible to calculate χ^2 for a grouping of this kind and size; $\chi^2=10{\cdot}87$, $P<0{\cdot}01$. The reasonable nature of the conclusion expressed as $P<0{\cdot}01$ is shown in Table 5, where of eighteen cases of the mixed-exposure kind but with unknown lengths of exposure to each hazard, only one case was diagnosed as papilloma, all the rest being malignant from the start (one not diagnosed at the start).

The implication from our records is that tumours of the bladder developed by men exposed to mixed amines each suspected of carcinogenic effects are very likely to be malignant at the start.

It may be recalled that Engel (1937) considered that the compounds to which workers were exposed had a certain influence on the type of tumour later developed. For instance, he thought β-naphthylamine more likely to give rise to papillomata and aniline and benzidine more likely to give rise to malignant tumours. It is difficult to conclude on this matter and we are loath to go further than the above statement in relation to mixed exposure which seems very strongly supported by our data.

With regard to the basic problem of whether the four amines are all tumour-forming, our data leave no doubt that men engaged on each of the processes do develop tumours. Whether the effects of α-naphthylamine are due to its undoubted content of the β-isomer, can finally only be settled by experiment and by manufacturing pure α-naphthylamine for a sufficiently long time. Experiment has hitherto been negative.

The question of aniline carcinogenicity has, as stated above, gone through various stages until now there is some doubt as to its possessing such a property. Experimentally, results have been variable, some workers having reported tumours of the bladder but the more sceptical have reported consistent failure. Cases reasonably attributable to aniline only are uncommon in our experience but it must be remembered that effective precautions can be and most often are taken in the manufacture and handling of aniline and its near homologues, as is shown by the relatively infrequent occurrence of cyanosis among the workers in them. Hardly a writer on this subject fails to present cases which must be attributed to aniline. The recent report of Billiard-Duchesne of a man who had worked on making mercaptobenzthiazole (*vide supra*) is of interest to us because quite recently we have noted a good deal of maintained microscopic hæmaturia among workers manufacturing rubber chemicals including mercaptobenzthiazole. This compound and others (for example, diphenylguanidine and diphenylurea) involves the exposure of men in greater or lesser measure to aniline. Provided other exposures can be held to be innocuous, cases arising among these men must be attributed to aniline.

Bladder tumour cases attributed to the benzidine process only are also relatively uncommon in our experience but of their reality there seems little doubt. By whatever process benzidine is made (Zn–NaOH reduction, electrolytic, Na–Hg method) cases have been described as occurring in it. Except nitrobenzene the only aromatic compounds arising in the process are hydrazobenzene, benzidine, small amounts of azo-benzene, azoxy-benzene, and diphenylene. Experimentally benzidine has so far failed to give evidence of carcinogenic action whether administered intraperitoneally, by mouth, as vapour, or by skin painting. Azo-benzene and azoxybenzene have not, as far as we know, ever been shown to be tumour forming: hydrazobenzene and diphenylene (2 : 4′ isomer of benzidine) do not appear to have been tested.

In the experiments with benzidine and aniline dogs do not appear to have been used. Since the most striking results on bladder carcinogens have been obtained with dogs, it seems desirable to use this species for testing other suspected bladder carcinogens in spite of the tedious and trying nature of such experiments. Benzidine is a much more acutely toxic compound than the naphthylamines so that dosage will probably present some problems.

Tumours Developed in Workers other than Process Workers : All Mixed Exposures.—In Table 6 we record briefly the cases of tumours detected in the two factories in the course of the last twelve years among workers who, whilst not engaged on process work in the usually accepted sense, were undoubtedly exposed to the suspected compounds. The

exposure of a fitter in a hazardous plant is obvious : a cooper might have to enter the plant to examine and remove faulty containers for repair and would, unless the containers were rigorously cleansed, come into close contact with a variety of residues of amines and derivatives.

TABLE 6

Cases	Age at death	Age now	Tumours
2 coopers	64	—	Carcinoma prostate
	73	—	Carcinoma bladder
3 fitters	71	—	Carcinoma bladder
	54		Carcinoma bladder
	—	41	Papilloma bladder —recurrent
1 cleaner and laundryman for 15 years	60	—	Carcinoma bladder
1 man working adjacent to β-naphthylamine plant	—	50	Papilloma bladder

Particular attention must be drawn to the laundryman and cleaner, whose only contact with the suspected amines must have come about by badly contaminated clothing. To launder such clothing in hot detergent fluids (some likely to be alkaline) is to come into contact with liberated bases, some of which are volatile in steam : opportunity for absorption of various compounds *per cutem* is great : a recent determination of the amount of amines in process men's clothes (benzol extraction and fractionation) showed that several grammes of naphthylamines were impregnated in the fabric. As the man in question died as long ago as 1938 it may be considered as certain that the clothes he handled were more heavily contaminated than they would be in the improved conditions since.

The last case in Table 6 is that of a man who developed a bladder papilloma at age 48 after twenty-nine years in the industry. He was stated not to have had direct contact with any of the suspected amines but to have worked at various times on processes adjacent to the β-naphthylamine process (e.g. β-naphthol).

This table of cases (six bladder tumours) is in itself far from insignificant, in the twelve years in which it grew up, as an index of the high incidence of bladder neoplasms in this industry.

Prognosis.—We have already stated that routine cystoscopy is not practised in the factories being considered ; reliance is placed on routine urine examination as a first sorting test, routine cystoscopy being carried out in hospital after the first diagnosis of a tumour by cystoscope and after operation.

It is recognized that in some cases the earliest appearance of a tumour may be missed and thus prognosis may be adversely affected. Whilst cystoscopy is not refused by a man who has once undergone operation as he is then apprehensive about possible recurrences, the position is quite different for a man who is symptomless and is dubious about the significance of even visible blood in his urine. To propose cystoscopic examination among workers in Britain at present would mean either mass evacuation of parts of the industry or a demand from all exposed men for a transfer to other work.

It must be emphasized again that the hazard of bladder carcinogens can only be properly and completely controlled by routine cystoscopy, as long as exposure to them continues.

In Table 7 the times of survival from first operation are given in seventy-two cases* in relation to the nature of the initial tumour.

The column heading " papilloma —→ malignant " means that the initial diagnosis was papilloma and it was later found that malignant changes had appeared either at the original site or elsewhere. The term " first operation " has reference to any procedure designed to destroy or remove a growth (diathermy per urethram or open, partial cystectomy, total cystectomy). Inoperable cases were subjected to such operations as implantation of radon seed and deep *x*-ray therapy.

To summarize survival data completely requires that all the patients should be dead. In the summary given in Table 7 the incompleteness is due to the varying periods during which the surviving cases have been followed to date. This is due mainly to the varying times since the first operation was performed (some as recently as 1947 ; others as long ago as over ten years), and in some cases to the disappearance of the patient.

Table 7 summarizes what we know of the seventy-two cases up till 1948. Thus, for the twenty-eight cases diagnosed as papilloma and operated, we see that four were dead and fourteen were still alive five years after the first operation. The remaining ten cases cannot be included in the five-year group since none has been observed for this time as yet. But for the three-year period after first operation we know that three were dead at that time and eighteen were still alive.

It will be noticed that for the papilloma cases only 7/28 were dead even after thirteen years ; for the frankly malignant cases 25/28 were dead after thirteen years ; for the cases later developing

*All those cases for which operation details were available.

malignancy 6/10 were dead after thirteen years; and for the inoperable cases 6/6 were dead in something over two years. It is manifest that the survival of the malignant cases is poor. Combining the malignant and papilloma ⟶ malignant cases it is seen that 50 per cent. (19/38) were dead in less than one year from the first operation, and almost 70 per cent. (26/38) were dead in five years.

Regarding the whole series of seventy-two operated cases we see that half were dead in something over five years, and almost two-thirds (44/72) were dead in thirteen years.

Since forty-four cases had died after thirteen years it is clear that twenty-eight cases still survive. Of these sixteen have survived at least five years, seven at least ten years, and three have survived over thirteen years. Of these surviving cases, twenty-one were initially simple papillomata.

It is relevant to note that the very early deaths recorded above were in some cases due to post-operative catastrophes, such as pulmonary embolism, paralytic ileus, or heart failure.

To determine a quantitative estimate of prognosis in terms of the nature of the tumours is extremely difficult, perhaps impossible, having regard to the following considerations:

(*a*) The disease is diagnosed and comes to treatment at very variable stages of development towards malignancy. (Routine cystoscopy would probably overcome this.)

(*b*) The tendency to recurrence is very marked in some cases, less so in others.

(*c*) Surgical treatment may be undertaken by surgeons of varying competence and skill. (Incomplete diathermy may accelerate tendency to malignancy.)

(*d*) The location of the tumour may determine a fatal outcome even when the latter is of relatively low malignancy.

The high proportion (twenty-eight out of seventy-two) of operated cases who died in about one year or less from the time of first operation is an indication rather of the advanced stage at which the tumour is first met with than of the ineffectiveness of surgical methods. In some few cases death was due to such calamities as pulmonary embolism or paralytic ileus.

We are loath to lay any stress on mean survival times, the range being from <1 to >13 years.

Given a reasonably early diagnosis, a location not involving the orifices, satisfactory renal function, and prompt surgical intervention at the non-malignant or pre-malignant stage, the prognosis of the first operation may be good enough for the patient to look forward to years of valuable working life. This depends, however, on periodic cystoscopic examination, the importance of which lies in avoiding the establishment of a tumour of malignant character.

Prognosis in an occupational disease cannot or should not be detached from the essential industrial criterion—that is, return to productive work. Treatment which prolongs life during its productive phase without, at the same time, making productive effort possible, cannot be regarded as having

TABLE 7

SUMMARY OF DATA AVAILABLE ON SURVIVAL TIMES FROM FIRST OPERATION ON BLADDER TUMOUR

Year(s) after operation	Nature of initial tumour								Total (72 cases)	
	Papilloma (28 cases)		Malignant (28 cases)		Papilloma ⟶ malignant (10 cases)		Inoperable (6 cases)			
	D*	S*	D	S	D	S	D	S	D	S
0–1	1	27	16	12	3	7	3	3	23	49
1–	1	27	19	9	3	7	5	1	28	44
2–	1	23	21	7	3	7	6	0	31	35
3–	3	18	22	5	3	6	6	0	34	29
4–	4	16	22	5	3	6	6	0	35	27
5–	4	14	23	4	3	6	6	0	36	24
6–	4	11	23	4	4	5	6	0	37	20
7–	5	9	23	4	4	5	6	0	38	18
8–	5	8	24	2	4	5	6	0	39	15
9–	6	6	24	2	5	4	6	0	41	12
10–	6	4	24	2	5	4	6	0	41	10
11–	7	3	24	1	5	3	6	0	42	7
12–	7	3	24	1	5	3	6	0	42	7
13–	7	1	25	0	6	2	6	0	44	3

*D = deaths. S = surviving cases.

(Repetition of figures in the columns signifies unchanged numbers of dead or surviving cases and not additional numbers of dead or surviving cases.)

succeeded although in its human aspect it may be most gratifying. Regarded from this point of view, *of the seventy-two cases given above some thirty were never able to return to work of any kind.*

Recurrences.—A characteristic feature of this disease is the tendency to recurrences of tumours. The phenomenon is one of sprouting rather than of recurrence, although occasionally new tumours appear at old sites. The destruction by fulguration of a localized tumour or perhaps an area of small tumours may be followed after an interval by a newly-sprouted tumour whether exposure to the carcinogenic compounds has continued or ceased.

In the following tabulation are given some examples of the periods at which recurrences were found.

Patient	*No. of recurrences*	*Successive periods (months)*
Ai	1	8
Ar	2	8, 36
Bl	4	15, 20, 15, 88
Geo	2	7, 21
Ke	2	2, 4
La	1	24
McN	1	48
Me	1	20
Mitch	4	16, 28, 11, 9
Rob	3	7, 3, 3
Uns	1	17
Walk	1	1
Whi	1	8
Wo	3	16, 5, 8
Br	1	<12
Car	1	6

This tendency is of very great importance especially in the case of men who, recovered from a first operation, decide to leave the industry and disappear from continued control.

Inasmuch as this tendency remains throughout the life of the affected person, it is apparent that the responsibility for compensation is a liability that can cease only on his death. To restrict compensation to a loss of faculty developed during employment in the hazardous processes or whilst liable to be affected by the dangerous compounds is to ignore the essential nature of the disease. Difficult as it would be in practice, the responsibility should be laid upon the men while continuing in the industry and after leaving it to present themselves regularly for appropriate investigation. To make such a proposal work it will be necessary to have every man engaged in these processes on a special list which would make it possible to identify and locate him and to trace his works history. It would be quite unfair to leave the worker the onus of obtaining advice for, with a furtive disease such as this, he is in many cases unlikely to suffer loss of faculty before it is too late to save him. If done in this way and with the assistance of persons expert in this disease, frivolous claims are not likely to arise. Corresponding obligations would fall on the employers, such as approved methods of works' medical control, organization of accurate record of nature and duration of certain categories of operation and process, introduction of approved methods of manufacture, approved methods of ablution and of amenities, approved types of works apparel and safety measures, regular determination of atmospheric conditions, and routine inspection of plant.

Parallel with all this, research should be carried out to circumvent the present need to manufacture the free carcinogenic bases.

Metastases.—It is not uncommon to find it stated, less nowadays than formerly, that occupational tumours of the bladder do not give rise to metastatic deposits. Whilst it is true that some cases of very advanced carcinoma of the bladder do not appear to be associated with metastases even when the pelvis is a mass of matted malignancy, it is certainly true that secondary deposits may be found in a certain number of cases, of a highly malignant kind. Table 8 presents some data on this point.

Other observers of this disease have described metastases in the vertebræ, brain, lungs, and liver, as well as in the lymph glands in adjacent or distant parts of the body.

Considering the (not inconsiderable) size of the present series, it is clear that metastases are relatively uncommon in this disease.

Tumours of the Excretory Passages other than the Bladder.—Tumours of the pelvis, ureter, or prostatic urethra are very rare compared with those of the bladder. This is true both for occupational and non-occupational tumours. Considering that these parts (calyces, pelvis, ureter, bladder, prostatic urethra) constitute both functionally and histologically a unit system, this fact is not readily comprehensible, but, we hold, more reasonably explained on the hypothesis of a urinary carcinogen. The blood-borne carcinogen theory seems inadequate to explain this fact since the blood supply to all those parts is very similar. The layers of epithelial cells in the pelvis and ureter are fewer in number than in the bladder so that it might be thought likely that the absolute amount of a systemic carcinogen which, issuing from the closely applied sub-epithelial capillaries, would come into contact with a given number of epithelial cells would be higher in these parts than in the bladder (assuming no great difference in the density of the capillary network). In the trigone the density of vascular supply is greater than elsewhere in the excretory passages and so might permit a greater

exposure of its epithelium to a systemic carcinogen. The bladder (even excluding the trigone) is incomparably more frequently the site of tumours than the ureter, pelvis, or prostatic urethra, a fact which demands some hypothesis more potent than the blood-borne carcinogen theory to explain it.

Whatever theory is adopted the rational explanation of tumours arising many years after exposure has ceased can only lie in one or more of the following :

(*a*) Modification of parts of the epithelium which in the course of years become neoplastic (some form of undetectable metaplasia during exposure).

(*b*) Modification of parts of the epithelium which renders the cells more susceptible to the attack of a carcinogen when the latter appears (this modification is a potentiation).

(*c*) Retention for years of minute amounts of the urogenous carcinogen in the bladder tissue, the ultimate tumour effect being delayed but inevitable (theory of direct amine carcinogen).

The fact that the process of tumour formation may begin as a sub-epithelial vascular reaction lends no support to either the systemic or urogenous theory, for sub-epithelial reactions of this kind can occur after amines are instilled directly into the bladder of animals or injected parenterally or given by mouth.

Support for the urinary theory rests largely on the anatomy and physiology of the excretory passages. The whole apparatus from the calyces and pelvis to ureter, bladder, and prostatic urethra is lined with *transitional epithelium* and is adapted to a simple process of collection and transmission of fluid, the bladder adding a more complicated process for expulsion. The funnel shape of the minor calyces and pelvis emphasizes the adaptation to the function of collection and transmission.

The estimated volume of the calyces and pelvis of one normal human kidney is about 8 c.cm. The rate of secretion from the kidney is subject to very wide variations. To permit such wide variations it is essential that the excretory passage shall not only offer no static obstruction but should assist in the disposal of fluid entering them from the renal papillæ. This latter is brought about by the provision of smooth muscle (two longitudinal and one middle circular layers) along the entire chain of excretory passages. The active participation of the smooth muscle system is visible cystoscopically when the ureters squirt out the urine into the bladder.

This process is continuous and in the normal subject the contact with the calyces, pelvis, and ureter is of very short duration for any particular volume of urine.

If, as we believe, the bladder carcinogen (or potentiator) is carried in the urine, the intensity of its action will depend on the concentration, the time of action, and the intimacy of contact with the cells. When the active agent passes over the calyces, pelvis, and ureter, intimacy of contact is certainly not obtained as it is in the bladder both between acts of micturition and after micturition when small residues of urine remain engaged in the rugæ in the bladder generally ; but in the trigone, which is firmly fixed and traversed by fine folds radiating from the internal urethral orifice, there is likely to be less intimate contact after micturition since the surface is smoother.

The very frequent location of the occupational tumours near the ureteric orifices calls for an explanation based upon some structural feature of this area. Inasmuch as the ureteric orifices form two of the apices of the trigone, the contribution made by the long contact with urine applies also to the

TABLE 8

Patient	Nature of primary tumour of bladder	Secondary growths
Beau ..	Inoperable cancer from dome to trigone	*Liver* riddled with large secondaries.
Mid	Semi-sessile tumours growing in lower end of ureters into lumen of bladder	*Lymph glands* showed secondary growth.
Mitch ..	Papilloma on posterior wall Carcinomatous mass on anterior wall	*Left kidney* showed area of secondary carcinoma and pyonephrosis.
Murph ..	Inoperable sessile infiltrating cancer	Enormous mass of malignant *lymph glands* in lumbar region. Mediastinum contained large mass of malignant glands—all transitional cell carcinoma. Nodule of secondary carcinoma in *left kidney*. Hydro and pyo-nephrosis.
Whi	Squamous cell carcinoma invading muscle coat	Right *inguinal gland*—carcinomatous.

ureteric region but an additional contribution is probably made by the presence of the plica ureterica which, with the adjacent rugæ can bring about a local relative stasis of urine.

The question of concentration is important. It can be shown that aromatic amines are excreted rapidly both by man and animals, that is, the concentration in the blood does not rise to high levels whereas the amine urinary concentration rises steeply and falls less steeply but rapidly. Thus, at a time when the calyces are receiving a urine of low or even indeterminable amine content, the bladder may still be in intimate contact with amine (and derivatives) excreted at earlier stages and may continue so for hours.

It is, we suggest, important not to assume that the conditions which the carcinogen (or potentiator) meets in the bladder are identical with those met with in the ureter, pelvis, and calyces. In the bladder the urine reaction may be different from that of "renal urine": it may contain bacteria, epithelial cells, yeast cells, mucus from the vesical glands, gaseous compounds derived from the lower gut. It is conceivable that such factors may have some bearing upon the selective attack on the bladder by the amines or active derivatives.

In the present series of cases primary tumours of the excretory passages other than the bladder were confined to one indubitable case. This was a man who entered the industry at twenty-three years of age, worked from age twenty-seven till the age of thirty-four in processes involving β-naphthylamine, and developed three bladder papillomata which were fulgurated *per urethram*. Some eight months later he was found to have a fresh papilloma near the left ureteric orifice, which was also fulgurated successfully. One year and eight months later recurrence of signs with negative cystoscopic examination led to the discovery of a new growth in the pelvis of the right kidney. The kidney and ureter were removed. Growing from the pelvis were two papillomata (fig. 5), one about the size of a table-tennis ball and the other about ½ in. in diameter. In addition, at the lower end of the ureter a small papilloma was found. These tumours were typical papillomata with no signs histologically of malignancy; the pelvic tumour was infiltrated with lymphocytes.

This was therefore, a case of papillomatosis with recurrences. The tumour in the kidney must have grown after the bladder tumours in view of the considerable period of freedom from signs or symptoms. The nature of the tumours leaves no doubt that they were primary. The tumours in the ureter may have been an implantation.

The occurrence of only a single case of this kind in the present series is, in our view, strong evidence that the carcinogen, whatever it may be, is urine borne.

Summary

1. The incidence of bladder tumours in two chemical factories in Britain is presented.

2. The following numerical characters of the disease emerge from analysis of the series:

Mean period from first entry into the industry till first discovered tumour:
18·95 years (S.E. 0·8) 100 cases

Mean age at first recognition of tumour:
50·55 years (S.E. 1·1) 93 cases

Mean age at death from tumour:
54·2 years (S.E. 1·35) 60 cases

Mean age at death in relation to age at first entry into the industry:

47·7 years (S.E. 1·8)—28 cases entering at less than 30 years of age

55·9 years (S.E. 1·7)—18 cases entering between 30 and 40 years of age.

67·1 years (S.E. 0·37)—13 cases entering between 41 and 52 years of age.

These data indicate that the earlier the industry is entered the earlier is death likely to occur *if a tumour is contracted.*

2. Comparison with the Registrar General's reurns of deaths due to tumours of the urinary tract shows that the proportion of deaths at ages less than 45 years due to occupational tumours of the bladder far exceeds that for urinary tumours in the general population.

3. Although, of the primary aromatic amines only β-naphthylamine has been shown experimentally to produce bladder tumours in dogs, evidence is presented that cases arise among workers who have been engaged not only exclusively in β-naphthylamine but also among others engaged exclusively in aniline, benzidine, and α-naphthylamine (containing small percentage of the β-isomer).

4. The present series of cases suggests that bladder tumours arising in workers who have been engaged in β-naphthylamine or in more than one of the amines mentioned are more likely to be malignant from the start than those arising in workers engaged in one only of these amines.

5. Figures are given showing the order of excretion of aromatic amine in the urine of workers engaged in the manufacture of α-naphthylamine.

6. Figures are given showing the survival times after operation hitherto recorded among the present series.

FIG. 5—Papillomata of renal pelvis in a chemical worker (see text).

7. Recurrences (freshly sprouted tumours in the main) are a feature of the disease and may appear from as little as a month or two after operation to as long as seven years after. Recurrences may appear long after leaving the industry.

8. Cases are recorded among workers who had been exposed in occupations ancillary to manufacture and use of the carcinogenic amines.

9. Metastases were found in only five cases of malignant disease of the bladder coming to autopsy. Metastases are thus relatively very uncommon.

10. Tumours of the excretory passages other than the bladder are very rare. One case of an undoubted primary tumour of the renal pelvis is described.

11. Brief indications are given of possible improvements in process operation which could contribute to elimination of the disease and which have proved valuable in practice.

12. It is held that the so-called amino carcinogens are only indirectly responsible for the tumour formation in that they sensitize or potentiate the tissue to the true carcinogen.

It is held that the amino potentiator (carcinogen as it is now called) is carried in the urine.

It is a pleasure to express my appreciation for their helpful efforts to Dr. C. Cresdee and to the managers and chemists in the factories concerned as well as to the urologists in the hospitals to whom the cases were submitted for cystoscopy and operation.

It is also a pleasure to express my grateful thanks to Miss Rachel MacHatton, B.Sc., for her great help in the preparation of this paper.

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MANGANESE PNEUMONITIS

FURTHER CLINICAL AND EXPERIMENTAL OBSERVATIONS

BY

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In 1837 Couper reported a case of manganese poisoning in a Glasgow stevedore, and accounts of the systemic effects of manganese in upwards of 250 industrial workers have appeared with increasing frequency since the 1914–18 war. The first suspicion that manganese might cause pulmonary disease was in 1921, when Brezina reported a high death rate from pneumonia in workers in a pyrolusite mill. After the opening in 1923 in Sauda, a small Norwegian town, of a works which smelted manganese ore, Elstad (1939) reported that the pneumonia rate was eight times higher in that district than in the rest of Norway. The increased pneumonia rate was associated with a pall of smoke which was emitted by the works and which consisted of dust containing manganese. Buttner (1939) observed a high incidence of deaths from pneumonia amongst Rhenish manganese miners who also suffered from silicosis as the Geissen ore contains about 20 per cent. of silica. Buttner agreed with Baader (1937) that the constant occurrence of pneumonia among manganese workers allowed of no other point of view than that manganese has a causal relation.

Because of the difficulty in reproducing the condition in animals, and from an analysis of the pneumonia rate of different groups of exposed workers, Heine (1943) doubted the direct relationship between manganese and pneumonia. Jötten and Reploh (1939) showed that though the inhalation of manganese induced pneumonia in rabbits, the presence of some other factor such as the inhalation of pneumococci or "twisting the rabbits about," in order, in the view of the authors, "to simulate extreme climatic conditions," increased the ease of production of pneumonia and its intensity. Reploh (1943) reported a similar result after mice had been exposed to the dust of manganese carbonate, dust from a Sieman-Martin's furnace containing 9 per cent. manganese, and basic slag. Though some lung changes occurred after exposure to dust alone, these were enhanced if the mice were treated with inhalation of dead pneumococci, or with dead pneumococci and live pneumococci eight days later.

Observations by Lloyd Davies (1946) showed a causal relationship of manganese to the high incidence of pulmonary disease experienced by a group of men (numbering over a period of eight years from 47 to 124) exposed to the inhalation of manganese dioxide and higher oxides of manganese. Besides a high incidence of pharyngitis, bronchitis, and bronchopneumonia, an illness commonly diagnosed as pneumonia occurred with a frequency of 26 per thousand compared with an incidence of 0·73 per thousand for pneumonia in a control group. As this illness showed slight clinical differences from pneumonia, but more especially as manganese affected the whole respiratory tract from the nose to the alveoli, the term manganese pneumonitis was suggested.

Environmental studies in the works showed that high total particle counts were frequent; very commonly dust counts (determined by the thermal precipitator) in the region of 5,000 particles and occasionally counts as high as 20,000 or more particles per c.cm. of air were obtained.

In all counts 90 per cent. of the particles were less than 1 μ, and nearly always 80 per cent. of particles were less than 0·2 μ. Calculation of the mass concentration gave results which differed widely from the mass concentration determined by the electrostatic precipitator (Lloyd Davies, 1946). Six estimations of the dust present in the air by the electrostatic precipitator gave concentrations of 0·42, 0·7, 7·9, 9·2, 37·3, and 38·3 mg. of dust in one cubic metre of air. The corresponding manganese dioxide content of the dust was 41, 43, 66, 65, 58, and 54 per cent. Flinn and others (1940), who observed thirty-four men working in a manganese ore-crushing plant, found no case of manganese

poisoning in nine men exposed to less than 30 mg. of manganese per cubic metre (though two had been exposed for less than a year). Of ten men exposed to inhalation of "manganese"* in concentrations of 90 mg. per cubic metre, five suffered from poisoning. Five out of six men suffered from poisoning after more than three years, and three out of four men after less than three (but more than one) years' exposure. Fifteen men were exposed to intermediate concentrations, and three were affected, though the varying work of each made exact determination of the risk difficult.

Under the conditions of the experiment mice exposed by Lloyd Davies (1946) to dust of manganese dioxide did not show an increased susceptibility to *Pneumococcus* type II or IV or to *Streptococcus hæmolyticus* (Richards), even though marked toxic effects, due to manganese, were present. A characteristic monocytic reaction constantly occurred in the lungs of exposed mice.

Clinical Observations

Table 1 is a continuation of Table 1 in Lloyd Davies' original communication (1946) and shows that the high incidence of manganese pneumonitis has been maintained.

In four cases of pneumonitis or pneumonia occurring in 1946 to 1948 the sputum or nasopharyngeal swabs were examined with the results shown in Table 2.

Though all patients were treated by chemotherapy, and the consequent alteration of the bacteriological flora of the sputum and nasopharynx makes interpretation of the result equivocal, it seems unlikely, with the exception of Case 3, that bacterial infection played a primary role in producing the consolidation unquestionably present in the lung.

Animal Experiments

Manganese in the form of manganese dioxide dust and of solutions of manganese chloride was introduced into the lungs of rats to determine (*a*) the histological changes developing over a period of time after the introduction of manganese dioxide, and (*b*) the immediate effect of manganese dioxide and chloride on the bronchial and alveolar epithelium.

Technique

A series of rats had manganese introduced into their lungs by intratracheal injection. Under ether anæs-

* Though Flinn and his collaborators do not specify the form in which manganese was estimated, it was probably as manganese dioxide.

TABLE 1

INCIDENCE OF PNEUMONITIS

Year	Manganese Plant			Health Insurance Society. Males 21–65 years			England and Wales (*b*)		U.S. Public Health Report Washington (*e*)
	Maximum number employees (at end) of any quarter)	Number of cases of "pneumonia"	"Pneumonia" rate per 1,000 employees	Number of male members	Number first certificate of pneumonia	Pneumonia rate per 1,000 members	Number reported cases of pneumonia (*c*)	Pneumonia rate per 1,000 population (*d*)	Pneumonia rate per 1,000 males
1938	47	3	63	5991	3	0·52	—	—	—
1939	40	2	50	6342	3	0·47	42,312	1·0	—
1940	67	1	15	6586	6	0·91	47,875	1·2	—
1941	101	3	30	6678	4	0·59	50,942	1·2	3·8
1942	124	3	24	6751	6	0·89	42,698	1·0	3·5
1943	101	2	20	4899 (*a*)	6	1·20 (*a*)	52,407	1·2	—
1944	70	0	0	5008 (*a*)	5	1·00 (*a*)	38,631	0·9	—
1945	75	2	26	4645 (*a*)	1	0·02 (*a*)	34,412	0·8	—
1946	94	1 (*f*)	10	4430 (*a*)	0	0·00	36,688	0·9	—
1947	99	3 (*g*)	30	—	Not available		—	—	—
1948 to date	—	1	—	—	—	—	—	—	—

(*a*) Civilians only.
(*b*) Summary Report by the Ministry of Health, 1942, and Annual Report H.M. Stationery Office.
(*c*) Males and females (all ages, including non-civilians).
(*d*) Population (estimated mid-year 1939) 41,460,000 (note, after 1939 statistics and estimates exclude non-civilian males).
(*e*) Public Health Report, 1943. Washington.
(*f*) One other case, not included in the Table, occurred in a man recovering and drying manganese dioxide in another plant.
(*g*) One patient developed heart failure and auricular flutter (see Table 2, Case 3).

thesia the trachea was exposed and a suspension of manganese dioxide dust (particle size, 80 per cent. of particles less than 1 μ), 10 mg. in 1 ml. normal saline was injected into the lungs through a fine needle inserted between the rings of the trachea. As previous work suggested that the immediate effect may depend on solution of manganese in tissue fluids, 1 ml. of 5 per cent. and of 0·5 per cent. solutions (*p*H 6·3) of manganese chloride in normal saline was injected into other animals. Animals were sacrificed at varying intervals, from one hour to eighteen months in the case of rats injected with manganese dioxide, and from a few minutes to eight days in rats injected with manganese chloride. After anæsthetization by ether, the trachea was tied during inspiration and the animal killed by cutting the abdominal aorta. The lungs were removed in an inflated condition and preserved in formol saline. To examine the bronchial and alveolar epithelium, the animal was killed with ether, and the lungs were removed immediately after death and distended by running a mixture of equal parts of formol saline and a saturated watery solution of mercuric chloride into the trachea under about 5 cm. pressure. Paraffin sections were stained with Ehrlich's acid hæmatoxylin and eosin, with Weigert's elastin stain and Van Gieson, and by Wilder's modification of Foot's method for reticulin : frozen sections were stained with Scarlach R. One of us (H.E.H.) reported on the histological sections without knowing the experimental details of the animals, all of which were injected by the other (T.A.L.D.) in the Research Department, Boots Pure Drug Co. Ltd. Reports were subsequently placed in their proper time relationship and found to form a series showing progressive changes. In all, seventy rats were injected and their lungs examined.

Results

After the injection of manganese dioxide,* areas of the lung varying in size and position according to the distribution of injected suspension were stained black and consolidated. Emphysema

* After the intratracheal injection of normal saline (*p*H 6·5) using the above techniques, the lungs of rats appeared normal and did not show any histological abnormalities.

TABLE 2

BACTERIOLOGICAL EXAMINATION OF NOSE, THROAT, AND SPUTUM

Year and Case No.	Interval between onset of illness and examination (days)	Result	Remarks
1946 (1)	4	Throat } *Staph. albus* and diphtheroid bacilli ; Nose } slightly haemolytic Gram-negative cocco-bacillus, probably *H. influenzae*. Sputum : No pneumococci. Culture : Gram-positive bacilli.	Own doctor's diagnosis, broncho-pneumonia
1947 (2)	9	Throat : Direct film : No pneumococci. *Strep. pyogenes.* Culture : No pneumococci.	Admitted to Nottingham General Hospital. Diagnosed lobar pneumonia. *X*-ray patches of increased density throughout left lung. Appearance suggests pneumonia with considerable pleural involvement.
1948 (3)	10	Throat : Culture : Many pneumococci. *Staph. albus* ; Gram negative bacilli. Nose : Culture : No pneumococci. *Staph. albus.*	Own doctor's diagnosis, atypical pneumonia, later developed heart failure with auricular fibrillation.
1948 (4)	4	Sputum : Direct film : Numerous organisms and few leucocytes. Culture : *Strep. haem. Staph. pyogenes. Staph. albus. Strep. haemolyticus. M. Catarrhalis.* Sarcinae. Pneumococci. Typing of pneumococci : The strain failed to give any agglutination or precipitation reaction with anti-pneumococcal serum types I, II, and III.	*X* ray of lungs : area of consolidation right lower lobe.

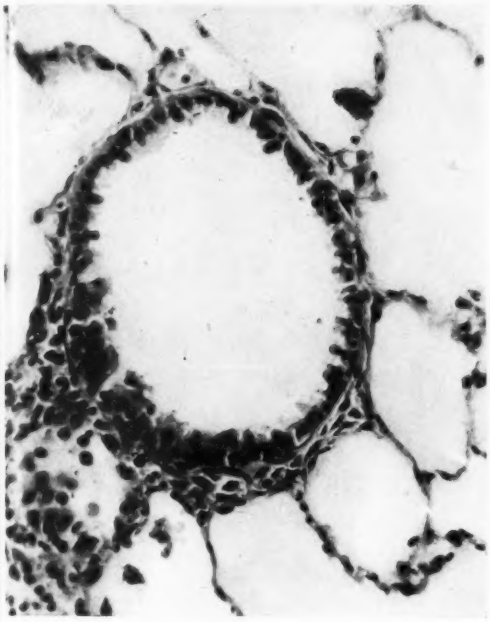


FIG. 1

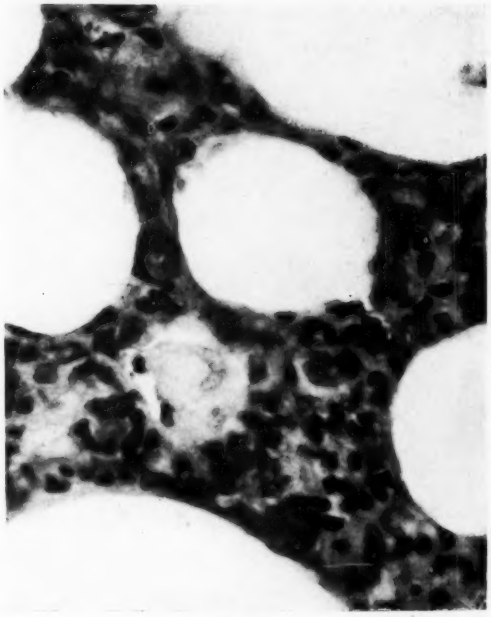


FIG. 2

FIG. 1.—Section of lungs of Rat 257, one hour after intratracheal injection of manganese dioxide dust. Alveoli are not evidently abnormal. Mucosa of bronchi (especially smaller bronchi) very ragged. Many cells have lost their supranuclear cytoplasm. ×350.

FIG. 2.—Section of lungs of Rat 10, four hours after intratracheal injection of manganese dioxide dust, showing irregular thickening of alveolar walls with mononuclear-cell infiltration and a few large hydropic cells. Bronchi (not shown) appeared normal. ×750.

FIG. 3.—Section of lungs of Rat 258, six hours after intratracheal injection of manganese dioxide dust, showing ragged bronchial mucosa. Cellular accumulation around terminal bronchi. ×500.

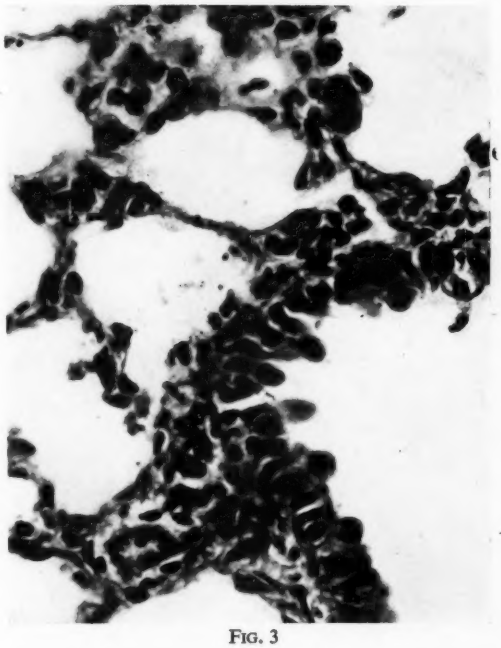


FIG. 3

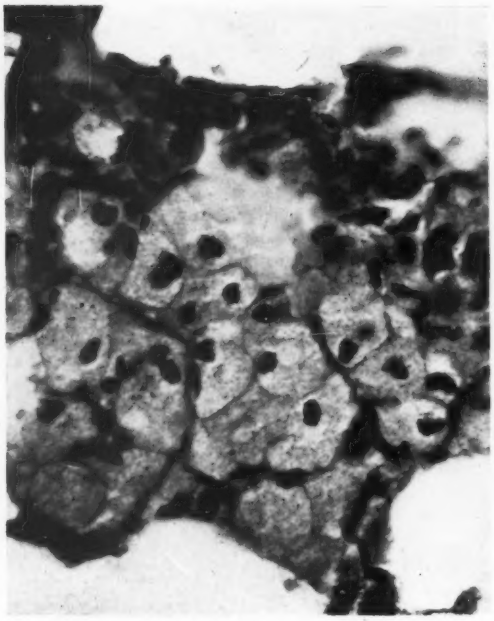


FIG. 4.—Section of lungs of Rat 1, twelve hours after intratracheal injection of manganese dioxide dust, showing mononuclear infiltration and many large hydropic cells filling adjacent alveoli. ×750.

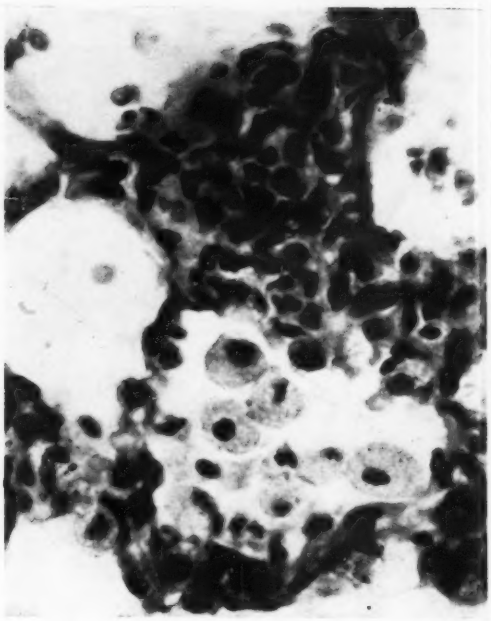
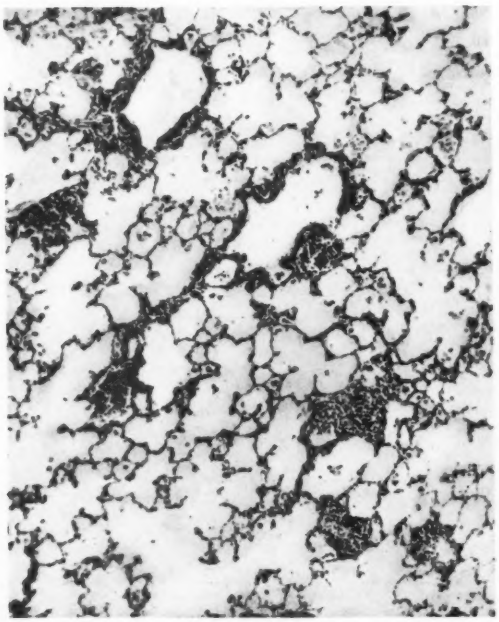
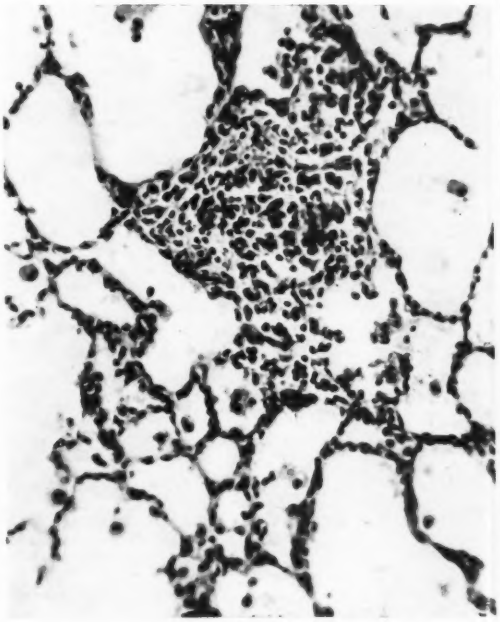


FIG. 5.—Section of lungs of Rat 5, seven days after intratracheal injection of manganese dioxide dust, showing similar changes to Figs. 2 and 4. Note mononuclear-cell reaction with no polymorphs. Alveoli filled with granular precipitate of protein (difficult to see in photograph). ×750.





FIGS. 6 and 7.—Section of lungs of Rat 262, fourteen days after intratracheal injection of manganese dioxide dust. Granular protein precipitate in alveoli, with mononuclear histiocytes (some with vacuolated cytoplasm) and large hydropic cells in alveoli. Suggestion of granulomatous follicles. Fig. 6 (left) ×40 and Fig. 7 (right) ×250.

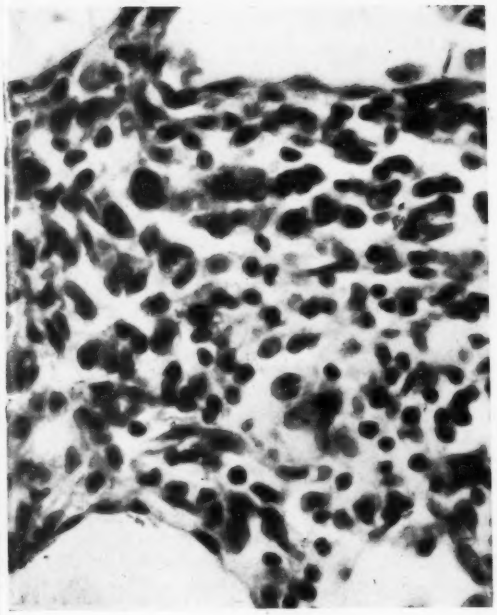


FIG. 8.—Section of lungs of Rat 263, twenty-nine days after intratracheal injection of manganese dioxide dust, showing granuloma with pigment filled histiocytes. ×750.

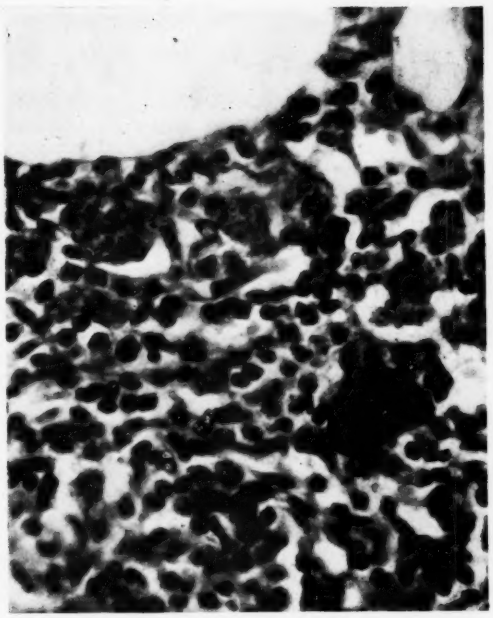
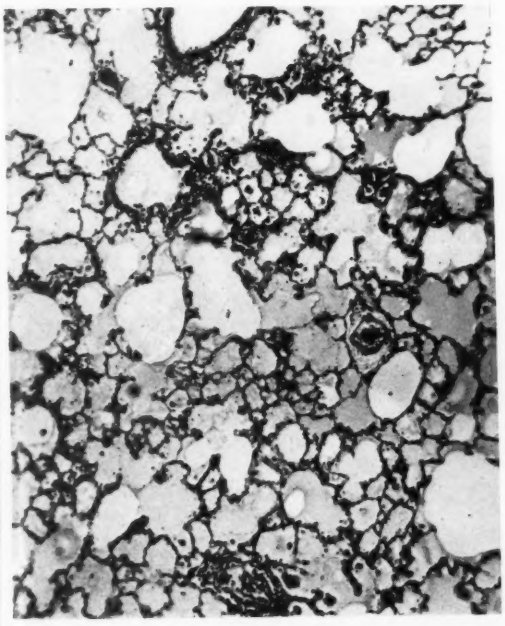
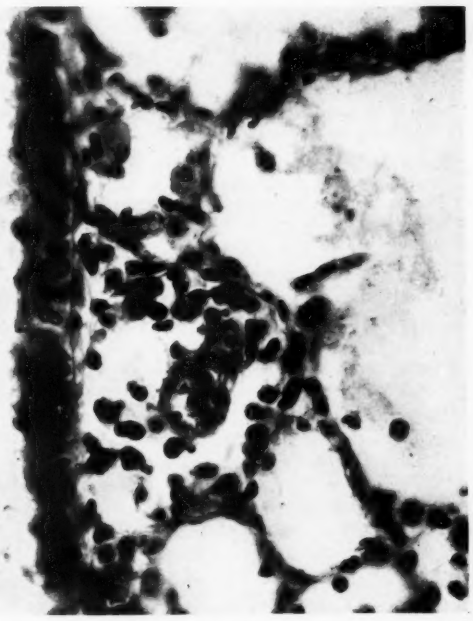
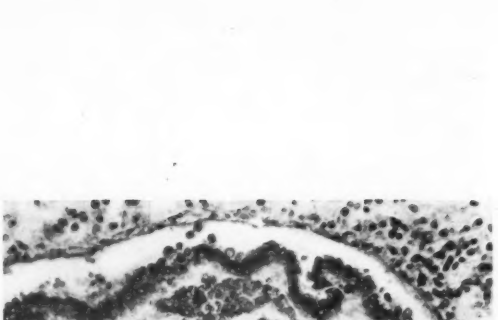


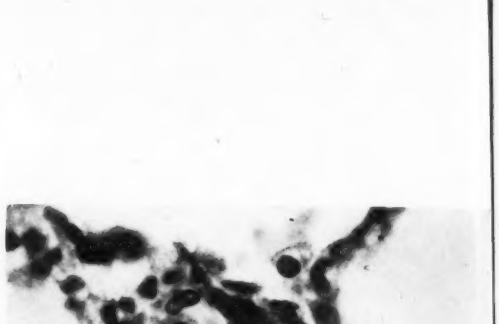
FIG. 9.—Section of lungs of Rat 68, three months after intratracheal injection of manganese dioxide dust. Pigment in masses enclosed within phagocytic giant cells, showing comparatively narrow rim of cytoplasm around margin. Macrophages show less pigment and seem to lie in nodal aggregates. Some alveoli are filled with large hydropic cells (not shown in photograph). ×750.





FIGS. 10 and 11.—Section of lungs of Rat 253, one hour after intratracheal injection of 0·5 per cent. manganese chloride solution. Alveoli contain eosinophilic coagulum showing occasional fibrils. Early cellular reaction (mostly mononuclear) at point where bronchi communicate with alveoli. Epithelium of bronchi covered by layer of mucus or balls of mucus; cells not evidently damaged. Fig. 10 (left) ×40 and Fig. 11 (right) ×500.





FIGS. 12 and 13.—Section of lungs of Rat 286 twelve hours after intratracheal injection of 0·5 per cent. manganese chloride solution. Most of the bronchial epithelium is detached from its basal membrane and lies coiled in the lumen. Alveoli contain a pale staining granular or fibrillar precipitate, and most contain one or more histiocytes. A few alveoli contain large hydropic cells. Red cells and debris are also present in the alveoli. Fig. 12 ×250 and Fig. 13 ×750.

appeared after a few hours. Histological examination shows that within fifteen minutes of contact with manganese dioxide the bronchial epithelial cells discharge their mucus, and their supranuclear cytoplasm shrinks and in some cases appears to be shed ; the mucosa, even at this early stage, has a very ragged appearance, with globules of mucus and portions of cytoplasm adhering irregularly to the surface. A little later shedding of the individual epithelial cells occurs, and short lengths of mucosa show loosening from the basal membrane. At this stage the alveoli show irregular inflammatory thickening of the walls. About twenty-four hours later a histiocytic (mononuclear) reaction appears in the interstitial tissue and the alveoli contain many histiocytic cells. This is characteristic of manganese. After four to six hours large hydropic cells with the nucleus pushed to one side by swollen cytoplasm containing fat droplets begin to appear ; after two days these cells may be present in large numbers. They are not specific to manganese as they appear after injection of silica, beryllium oxide, nickel oxide, and cobalt oxide, though in far fewer numbers. Similar cells occur in cats' lungs after the injection of suspension of manganese dioxide dust. Later wide-spread bronchopneumonia may develop and there may be a polymorph reaction. (The introduction of bacterial infection, either with the injection or secondarily, cannot be excluded.) Nevertheless, even in the case where a polymorph reaction does occur, the histiocytic reaction remains intense. At this stage the bronchial mucosa appears taller and has become less abnormal. Inconstant appearances after the injection of manganese are an early granulomatous reaction after a fortnight and phagocytic giant cells six weeks later.

After the injection of 5 per cent. solutions of manganese chloride all animals died of gross pulmonary œdema within a few minutes. The lungs were intensely congested, but histological examination showed nothing abnormal. Within an hour after injection of 1 ml. of 0·5 per cent. manganese chloride (*p*H 6·3) one third of the animals died from pulmonary œdema with a thin, watery fluid exuding in large quantities from their mouths. The lungs of animals dying or killed at this time are intensely congested. On histological examination the lungs of animals dying or killed a few hours later, show a protein precipitate in the alveoli, appearing mainly as a homogeneous eosinophilic coagulum but partly as a granular or slightly fibrillar precipitate. There is some proliferation of cells that appear to be histiocytes in the walls of the terminal bronchi and atria. The bronchial epithelium is cubical, the cells having discharged all their mucus. Animals killed or dying several hours later show rather less protein precipitate in the alveoli, which also contain a few histiocytes and, rarely, one or two polymorphs : the accumulation of cells is more marked in the region of the terminal bronchi. The bronchial epithelium appears disorganized, and much of it may be detached from the basal membrane and may be lying curled up in the lumen. Mucus and balls of epithelial cells cover part of the bronchial epithelium. In animals killed a week after injection the alveoli appear normal, but the mucosal cells of the small bronchi are still abnormal and contain less than the normal quantities of mucus ; and some of them are being shed.

Discussion

The results reported here differ from those of Continental workers as both in men and in animals manganese caused intense pulmonary irritation without the presence of other factors. Unlike Continental workers, who constantly report toxic symptoms, no case of systemic manganese poisoning was seen in spite of the closest watch.

In the group of workers observed by Lloyd Davies (1946) the particle size of the dust was very fine ; though the amount of manganese dioxide present in the air was determined on only seven occasions, the concentration was relatively low. The high particle count and low mass concentration is accounted for by the fact that the mass of a sphere or particle of dust assumed to be a sphere increases in proportion to the cube of the radius ; for example, 20,000 particles of manganese dioxide 1 μ in diameter have the same mass as 20 particles 10 μ in diameter. For this reason the workers observed by Lloyd Davies did not absorb a sufficient quantity of manganese to cause systemic poisoning, but because of their fineness the particles were particularly liable to give rise to pulmonary effects. Continental workers report neither studies of working conditions nor the number and size of particles of manganese dust present in the air.

Therein lies the source of confusion. No doubt if the particle size of the dust is larger, as is probable in the cases observed by Continental workers because of consistent reports of systemic poisoning, the chance of intimate contact with the epithelium and therefore of pulmonary symptoms will be less. In these circumstances, some other factor such as exposure to abnormal climate or bacteria, may be required to produce " pneumonia." The possibility of atypical pneumonia or virus pneumonia occurring in workers subject to the present observations cannot be entirely excluded. The constant occurrence of manganese pneumonitis, year after year,

and the clearly demonstrated irritant action of manganese in animal experiments in whom no suggestion of virus infection arises, renders this explanation very unlikely. The present series of animal experiments in which manganese was injected into the lungs of rats confirms that manganese is irritant to the bronchial and alveolar epithelium and causes a characteristic mononuclear-cell reaction. The intensity and nature of this reaction is unlike that seen after the injection of other dusts employed by us. Large hydropic cells constantly occur in large numbers after the introduction of manganese into the lungs of rats; less constantly, and in far fewer numbers, similar cells occur after the introduction of other dusts. Probably the presence of hydropic cells is related to the degree of tissue irritation produced by chemical agents. Further work on the significance of these cells is in progress. Histological appearances after the injection of manganese dioxide and manganese chloride into the lungs of rats leave no doubt that manganese causes a specific and characteristic cellular reaction, resulting in gross consolidation. Apart from the occasional accidental introduction of infection, no other factor is or can be operating. The conclusion is justified that, in man and animals, manganese dust in suitable particle size introduced into the respiratory system will, without the presence of other factors, cause pneumonitis.

Summary

Pneumonitis has continued to affect men exposed to the inhalation of dust containing manganese dioxide and the higher oxides of manganese. The intratracheal injection of suspensions of manganese dioxide in normal saline and solutions of manganese chloride in normal saline into the lungs of rats causes characteristic histological changes. Within fifteen minutes of contact with manganese dioxide the epithelial cells of the bronchi discharge their mucus and the epithelium becomes ragged and may be loosened from the basal membrane. An intense mononuclear-celled infiltration of the alveolar walls and alveoli develops after about twenty-four hours, and shortly after this large hydropic cells appear, often in large numbers. Late and inconstant changes are a granulomatous reaction and giant-cell formation. After about a year these changes have disappeared and the lung appears normal. The injection of manganese chloride causes intense congestion of the lung; many animals die from pulmonary œdema. The bronchial epithelium is disorganized and often detached, but compared with the effect of manganese dioxide the histiocytic (mononuclear) infiltration of the alveoli is less intense.

In man and animals, manganese dust in suitable particle size introduced into the respiratory system will, without the presence of other factors, cause pneumonitis.

We are indebted to Miss E. Wilkinson and Miss E. Parker for technical assistance in many tedious experiments and to Mr. T. C. Dodds for the photomicrographs.

Drs. Furness, Hay-Heddle, Hill, and O'Donovan have kindly allowed one of us (T.A.L.D.) to examine patients in their care.

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CHANGES IN THE LUNGS PRODUCED BY NATURAL GRAPHITE

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Graphite or plumbago is a crystalline form of carbon which occurs in nature as soft black masses or, less commonly, as crystals in igneous rocks: this natural graphite contains varying proportions of other minerals. Graphite is also made artificially from coke, and the best preparations of this kind are nearly pure carbon. This paper will deal with some of the effects of natural graphite, and the term "graphite" will be used to mean "natural graphite," that is, a mixture of minerals, largely crystalline carbon.

The main sources of graphite in 1935 were the U.S.S.R. 39 per cent., Korea 21 per cent., Germany 10 per cent., Austria 9 per cent., Ceylon 7 per cent., Madagascar 5 per cent., and Mexico 3 per cent. (Jones, 1943). During recent years the graphite used in Great Britain has come mainly from Ceylon and South-west Africa, but there has also been a small quantity mined in Borrowdale, Cumberland.

Not much more than 10 per cent. of the graphite produced in the world is used in pencils and crayons; more than half of it is employed in foundries and in making crucibles for metallurgical purposes. Finely ground graphite is used extensively as a lubricant, either alone or in combination with oil or grease: considerable quantities of the poorer quality graphite are used in paints and pigments for protecting metallic surfaces from various corroding substances—for example, stove polish, which consists of graphite mixed with some amorphous carbon and a little grease. Graphite is also used for making electrodes and dynamo brushes, and in dry batteries.

For most purposes graphite has to be ground to a fine powder, and there is a small industry devoted to grinding graphite which it supplies to commercial users. In other cases the grinding is done as a subsidiary process by firms who themselves use large quantities of crushed graphite. The method of grinding varies according to the fineness of the powder desired. In the past the general practice was to grind the graphite in an open-edge runner mill or in a ball mill, and this method is still in use in some factories where extreme fineness is not required. The more modern method of grinding is in a totally enclosed mill with automatic feeding and discharge. The older methods of grinding, mixing, and bagging graphite produced very large quantities of dust which floated in the air and reduced visibility often to a few feet, but there is relatively little dust in the few modern factories. It is the purpose of this paper to show that serious damage to the lungs can and does result from the inhalation of this dust, and to suggest that the minerals other than carbon found in it are largely responsible for these effects.

The mining of graphite, at any rate in Ceylon, seems to carry only a very small risk of pulmonary damage (Dassanayake, 1948) since the drilling is usually done wet, but radiographic changes without physical disability have been detected in some miners who have worked underground for more than twenty years. Radiographic changes are found earlier, are more marked, and tend to be associated with physical signs in workpeople engaged in curing graphite in Colombo.

Koopmann (1924) described the lungs of a man who had worked for fifty years in a graphite mill, and who was killed by accident. The lungs showed pneumoconiosis and cavities due to necrosis; there was chronic interstitial pneumonia, peribronchiolitis, and a nodular type of arteritis. This man, however, had had periods of employment as a stone-grinder, and this history, together with the fact that Koopmann saw nothing to make him suspect silicosis, led to little notice being taken of the

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report. The marked radiological changes that can be found in grinders and mixers of graphite were demonstrated by Dunner (1945) and by Dunner and Bagnall (1946). Dunner recorded his findings in five men, all from the same works, who had been handling graphite in the manufacture of stove polish for from seventeen to thirty-four years, and whose films showed reticulation and nodulation in varying degree, and in some cases massive shadows. One of these men (Case 2) showed a massive reniform shadow in the right upper zone and two large fainter shadows in the left lung: this case was again recorded by Dunner and Bagnall in more detail after the patient had developed a distinct cavitation of irregular shape within the opacity in the left upper zone of his lungs. This man has since died, and a description of his lungs will be given in this paper together with some details of another workman from the same factory who died in 1932, and a report on the lungs of a man who had been employed for over twenty years in grinding graphite, mainly from Ceylon, for another firm. The graphite to which the first two workmen had been exposed was mainly Korean.

Composition of Graphite

In his original paper Dunner was misled by the statement of the workmen that they used only "pure graphite" into believing that crystalline carbon might be responsible for the changes; in fact the graphite was "pure" only in the sense that it was not adulterated after being mined. This error was recognized in the later paper of Dunner and Bagnall, who gave some figures of the composition of a finished product from the man's works.

Three samples of Ceylon graphite and one each from South-west Africa and Korea have been supplied by the firm, together with a sample of "carbon black" which is mixed with the graphite in the final product. The ash after incineration at 600° C. ranged from 12·81 to 33·26 per cent. of the various graphites, but was only 0·34 per cent. of the carbon black. The graphites contained from 8·0 to 18·6 per cent. total silica, 3·6 to 10·0 per cent. free silica, and 0·8 to 4·5 per cent. iron. Analyses by *x* rays gave figures for crystalline silica slightly greater than those found by chemical methods. It is evident, then, that graphite is a very variable mineral only two-thirds of which may be carbon, and that it contains, among other impurities, notable quantities of crystalline silica.

Case Records

Case 1.—J.T. died in 1932 when 58 years of age. He had for sixteen years been employed in emptying 1½ cwt. sacks of black lead into a mechanical mixer from which the powder was shovelled into a rotary sieve. His foreman agreed that the work was very dusty, but denied that any other workmen suffered any disability. He had not worked for fourteen months before his death and had been confined to bed most of this time. His doctor said that he had a catarrhal condition of his lungs with a severe cough, which later became very severe and was accompanied by a large quantity of very black sputum. Post-mortem examination showed both lungs bound to the chest wall and extensively fibrosed: there was no evidence of tuberculosis or of bronchiectasis. The cause of death was given at the inquest as "heart failure from fibrosis of the lungs through inhaling a black substance while following his occupation" (*Hull Daily Mail*, Sept. 27, 1932). As far as can be ascertained this was the first report of a post-mortem examination of a graphite worker in Great Britain.

By the courtesy of Dr. J. C. Lees, histologist to the Royal College of Physicians of Edinburgh, I have been able to examine four blocks of tissue from this man's lungs. The sections show intense anthracosis. Two of the blocks show marked focal emphysema (fig. 1), while the other two show very considerable fibrosis, both diffuse and in the form of nodules that are highly suggestive of silicosis (fig. 2). There is peribronchial and perivascular fibrosis: the latter involves the wall of several vessels in which there is also considerable intimal thickening. There is diffuse black pigmentation throughout the densely fibrous areas, but less in the nodules: phagocytic cells filled with pigment also crowd some alveoli and plug some of the smaller bronchi. There is some purulent bronchitis, but no evidence of tuberculosis. Most of the black pigment has disappeared in incinerated sections but a small proportion of it is obviously iron: there is a fairly marked dusting with refractile silica particles throughout the fibrous areas.

Case 2 (This is the man whose radiographs were described by Dunner).—H.D. aged 67 years, was employed as a barman until he joined the Army in 1902. On leaving the Army in 1920 he worked on a graphite mill grinding Korean graphite until 1939, when he became unfit and was given light work involving no dust hazard. In 1947 he had lost over 2 stone in weight, and suffered from marked dyspnœa: he had very little sputum and not much cough. There was dullness to percussion in the right sub-clavicular region. A radiograph of his chest showed a massive homogeneous opacity in the right upper zone, a small rounded opacity overlying the lower part of the root of the right lung, a homogeneous opacity of less density in the left upper zone, a rounded opacity the size of a golf ball overlying the left root and the left cardiac border, and a fine mottling in the mid-zones of both lungs.

He died on April 9, 1948, and an autopsy was performed on behalf of the coroner by Dr. N. T. Whitehead. There were some adhesions between the upper parts of each lung and the chest wall. Small collections of black pigment, similar to graphite, were to be seen in the pleural lining of the chest wall: this pigment was also found throughout the lungs, which were jet black. On palpation there was a firm fibrous mass in each of the

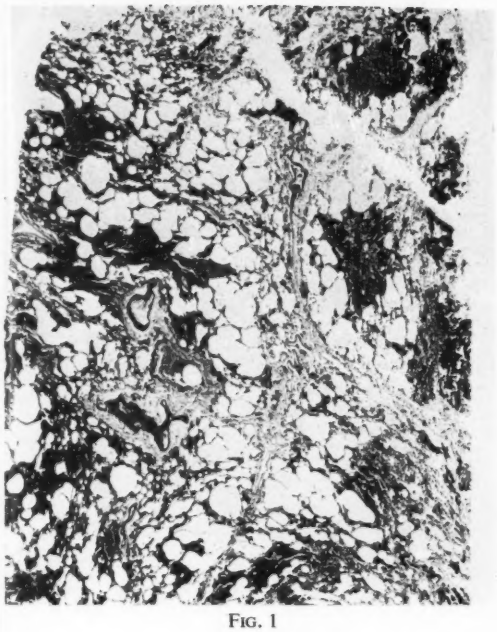


FIG. 1

FIG. 2

FIG. 3

FIG. 1.—Focal emphysema around pigment aggregates. Case 1. ×5.

FIG. 2.—Silicotic nodules and diffuse dust fibrosis. Case 1. ×5.

FIG. 3.—Right lung of Case 2. ×½.

FIG. 4.—Left lung of Case 2, $\times\frac{1}{2}$. This and Fig. 3 are deliberately light prints in order to show detail; the lungs are much darker than the photographs suggest.

FIG. 5.—Focal emphysema around pigment aggregates. Case 2. $\times 5$.

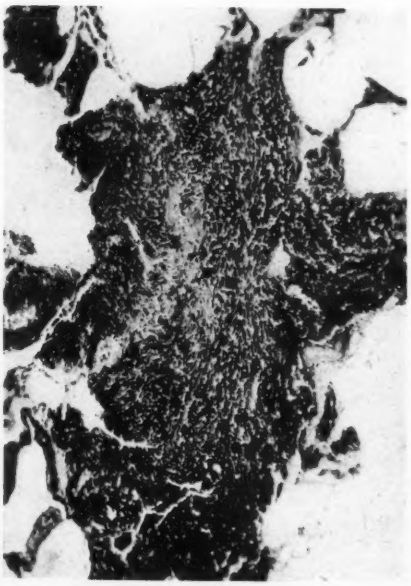
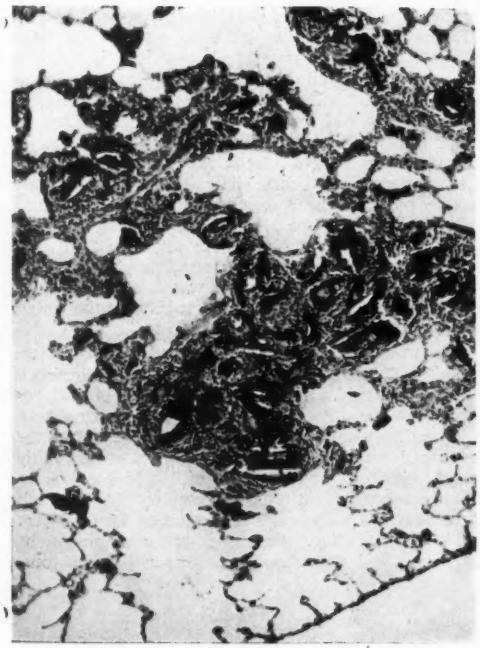


FIG. 7 (above).—Linear dust fibrosis. Case 2. $\times 32$.

FIG. 6 (left).—Protein precipitate in alveoli. Dust fibrosis. Case 2. $\times 10$.

FIG. 8.—Border of large cavity. Case 2. ×5.

FIG. 9.—Early necrosis in the middle of a medusa-head area of dust fibrosis. Case 2. ×10.



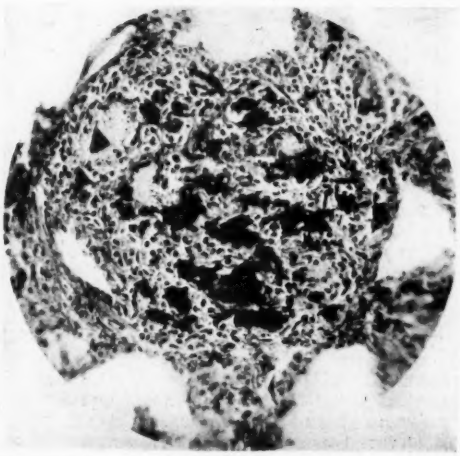


FIG. 11 (above)—Granulomatous nodule in lung of rat. ×180.

FIG. 10 (left).—Lung of rat killed nine months after intratracheal injection of Korean graphite. ×85.

lobes of the lungs: in the upper lobes these masses reached to within two inches of the apices: in the lower lobes they were more central: all were approximately $2\frac{1}{2} \times 2\frac{1}{2} \times 3$ inches. In the centre of each mass necrosis had occurred with the production of a cavity which had a black ragged wall and was filled with black semi-fluid material. There were also three fibrotic nodules approximately half an inch in diameter, one in the right upper lobe, one in the right lower lobe, and one in the left lower lobe. There was no evidence of tuberculosis. Between the œsophagus and the trachea were black, moderately enlarged lymph nodes. The heart muscle was soft and flabby. The left coronary artery was much narrowed by atheroma. Apart from the kidneys, which showed atherosclerotic changes, the abdominal organs and the brain appeared normal.

After fixation in formalin the right lung showed dense fibrous thickening of the pleura over the middle lobe and the lower part of the upper lobe, the rest of the pleura showed raised white lines, evidently corresponding with the pleural lymphatics, dividing up the otherwise black surface into irregularly shaped areas. The cut surface (fig. 3) showed that most of the upper lobe, all the middle lobe, and an area approximately $1\frac{1}{2}$ inches in diameter in the lower lobe adjoining the middle lobe, were either completely solid or consisted of dull black necrotic material some of which had fallen out. There was no interlobar pleural space, the middle lobe being recognizable only from the grey-white bands of fibrous tissue representing the original pleura. The cavities containing necrotic material were bounded in much of their circumference by a thin band of light grey fibrous tissue; elsewhere they abutted on dull black completely solid areas in which no fibrous tissue could be seen by the naked eye. Within the necrotic areas were irregularly shaped small portions of white tissue that represented the remains of pulmonary vessels. The rest of the lung showed numerous areas of dull black pigmentation which tended to run together in the middle of the lower lobe. The more peripheral pigmented areas showed well-marked focal emphysema but the central ones tended to be solid. The left lung (fig. 4) was essentially similar to the right. The large cavity in the lower lobe had a somewhat thicker and more complete grey fibrous capsule than those elsewhere. In the apex and posterior portion of this lower lobe it was possible to see bronchopneumonic exudate.

Chemical examination of the lungs showed that, of the dry weight, ash formed 5·65 per cent., total silica 1·14 per cent., free silica (method of Trostel and Wynne, 1940) 0·56 per cent., and iron (as Fe_2O_3) 0·98 per cent.

Histological examination showed widespread focal emphysema (fig. 5) which was somewhat masked by œdema (fig. 6), some purulent bronchitis and bronchopneumonia, but nothing that was even suggestive of tuberculosis. There were very many small areas of linear and radial fibrosis (fig. 7) but nothing resembling the classical whorled silicotic lesion. The large cavities (fig. 8) were bounded by a relatively narrow zone of dense fibrous tissue within which was an irregular wider zone of fibrosis so densely pigmented that it was almost impossible to make out its structure: inside this zone was deeply pigmented necrotic material that was mainly finely granular but showed also larger black particles of irregular rectangular shape and of the order of 25 to 40 μ by 2 to 4 μ: these were too black to show any possible staining with potassium ferrocyanide and HCl; they disappeared on incineration, and were taken to be graphite. There were also present some colourless crystals, found best in frozen sections, that were visible in polarized light and appeared to be cholesterol. An earlier stage of the necrosis is seen in fig. 9, which shows some of the spaces left by these crystals. In the earliest stages found the collagen fibrils in small areas showed only very faint staining with either eosin or van Gieson and were more swollen than the normally stained fibrils with which they were continuous. Vascular changes in the larger fibrotic areas were easily found in sections stained for elastin: they were similar to those pictured by Stewart and Faulds (1934) and by Geever (1947): many of them had progressed to complete obliteration of the lumen of arteries. Black pigment was widely distributed in large amounts, a little of it in phagocytes within alveoli, more within alveolar walls, and much more within the areas of fibrosis. Incinerated sections showed that most of this pigment was combustible, but a small proportion of it was iron. Incinerated and acid-treated sections showed a conspicuous dusting with refractive silica particles within the areas of fibrosis.

Case 3.—C.W., aged 71 years, up to the age of 40 had worked as a shoemaker. He then obtained employment grinding graphite (Ceylon and Madagascar) in an open-edge runner mill for five years. Then followed a break of three years when he worked on the delivery vans, after which he resumed work on a ball mill grinding graphite and continued at this job until five years before his death, when he ceased work owing to severe shortness of breath. His total exposure to graphite was thus about twenty-two years. When examined in 1946 he was pale and showed slight cyanosis of the lips and some dyspnœa at rest. He said that his cough was severe in the mornings and produced black sputum. A radiograph of his chest showed diffusely scattered shadows of irregular form in both lung fields. The right lung had an appearance of coarse reticulation with irregular patches of coalescence. The whole of the left upper and mid-zones was occupied by denser irregular shadows with coalescence but no definite nodulation. In the left mid-zone was an appearance suggesting a cavity with rather dense walls. Emphysema was seen at both bases and generally throughout both lungs between the denser areas.

This man died on May 7, 1948, and a post-mortem examination was performed for the coroner by Professor P. L. Sutherland. There were old dense pleural adhesions between the lungs and the chest wall on both sides and old adhesions to the diaphragm. Over the lower and outer part of the left lung there were fairly recent adhesions to the chest wall and also recent adhesions to the pericardium. There was fluid in both pleural cavities. The anterior margins of the lungs just met in the middle line. Both lungs were very voluminous and heavy and were emphysematous and œdematous.

The left lung was covered practically all over by thickened pleura: some of the thickening on the lateral lower aspect was fairly recent: the sulcus between the lobes was obliterated by adhesions. The surface of the right lung showed scarred depressed and puckered areas. In both lungs large masses and nodules of dense fibrosis could be felt: on the cut surface of the lung these appeared as jet black areas in some of which there were small cavities. There was no evidence of tuberculosis. Purulent secretion could be expressed from the bronchial tubes on the cut surface. The lung tissue was very black. The glands at the bifurcation of the trachea were enlarged and black but were not hard. The right ventricle of the heart was hypertrophied. The cause of death was silicosis and anthracosis.

A large portion of each lung was received from Professor Sutherland for chemical analysis and microscopical examination. Incineration at 600° C. had to be repeated several times before all the carbon was oxidized. The ash formed 7·56 per cent., total silica 1·77 per cent., free silica 0·47 per cent., and iron (as Fe_2O_3) 1·07 per cent. of the dry weight of the lung.

Histological examination showed generalized emphysema and œdema. There was marked pneumoconiosis showing as linear and radial collagenous fibrosis, and also diffusely scattered nodules of whorled hyaline fibrosis 1 to 3 mm. diameter closely resembling silicotic nodules. There was considerable black pigment, a little of it in phagocytes within alveoli, but mainly in the bands and zones of fibrosis and around the hyaline nodules. A small amount of the black pigment was of irregular rectangular shape up to 30 μ long. Incinerated sections showed that a small proportion of the finer black pigment was iron; the larger irregular particles burnt away and were presumably graphite. Incinerated and acid-treated sections showed a notable dusting of silica visible in polarized light in the areas of fibrosis. The hilar lymph glands showed marked black pigmentation mainly within phagocytes: there were large areas of diffuse collagenous fibrosis in and around the collections of pigmented cells, but no nodular whorled fibrosis.

Other Workers.—Most of the workmen employed at the factory at which Cases 1 and 2 had worked were examined in 1946, and radiographs were taken of their lungs. No men who had less than ten years' exposure to graphite showed any abnormality: all but one of thirteen men whose radiographs showed abnormal shadows had had over twenty years' exposure. Only two of these thirteen were unfit for work (one of these was Case 2), and it was notable that physical disability was on the whole small even in workmen whose radiographs showed marked changes. Brief notes of six of the men follow.

S.A., aged 52 years, had spent twelve years mixing graphite and twenty-two years grinding it. He had severe dyspnœa and was unfit for work. His radiograph showed a diffuse reticular opacity over the whole of both lung fields: the right lung was contracted, especially in its upper part where an irregular patchy opacity at the periphery suggested an area of pleural fibrosis.

G.J., aged 62 years, had worked in the graphite mill for forty-one years. He suffered from morning cough and from dyspnœa on exertion, but was still at work. Radiography showed a large homogeneous area of consolidation in the upper zone of the right lung with confluent opacities extending to the hilum: the mid- and lower zones of this lung showed pin-head stippling with small patches of confluent opacity. In the left lung was a large homogeneous opacity occupying the apical and infraclavicular region: there was accentuation of the root shadow, and pin-head stippling in the mid-zone.

A.S., aged 44 years, had been grinding graphite for twenty years. He was symptomless, but did not look fit. Radiography showed a diffuse opacity in the upper zone of the right lung with patches of greater density in the first and second interspaces; some mottling by indefinite spots of varying size in the mid- and lower zones, and a general increase in linear markings. In the left lung there was increase in the linear markings with accentuation of the root shadow: linear streaks of increased density fanned outwards from the upper part of the root: there was some indefinite mottling in the mid-zone.

S.J.W., aged 56, was symptomless apart from occasional slight cough after 25 years in the graphite mill. His radiograph showed confluent opacities in the upper zone of the right lung with coarse mottling in the mid-zone: there was patchy opacity with some linear infiltration in the mid-zone of the left lung.

R.W.C., aged 59 years, had worked for twenty-one years in the graphite mill, was symptomless, and felt quite fit. In his right lung radiography showed reticulation and fine mottling in the mid- and lower zones with patchy areas of confluent opacity in the upper zone. In the left lung were a few small scattered nodules varying in size and in sharpness of definition, mostly in the mid-zone.

H.O., aged 56 years, had been grinding graphite for twenty-six years: apart from a very infrequent slight cough he was quite fit. His radiograph showed reticulation (ground-glass appearance) throughout both lungs, most marked in the mid-zones.

The only three men who had been employed for over twenty years at the factory where Case 3 had been employed were examined in 1946. None of them had any physical disability; the radiographs of all three showed reticulation, and one of them showed also nodulation in the right mid-zone.

Animal Experiments

Under ether anæsthesia intratracheal injections of approximately 50 mg. of various samples of graphite from the factory where Cases 1 and 2 had been employed were given to groups of three-months old rats. The animals were killed six to nine months later, and the thoracic organs with the lungs in a state of normal inflation were fixed in formol-saline. Sections were stained with Ehrlich's hæmatoxylin and eosin, with Weigert's elastin stain and van Gieson, and by Wilder's modification of Foot's stain for reticulin fibrils.

No essential differences were seen between animals given different varieties of graphite. The surface of the lungs had a peculiar whitish appearance that seemed due to fine emphysema. Pigment was distributed fairly evenly throughout the lungs in small black areas: a few black dots showed in the pleura. Microscopically (figs. 10, 11) there was a marked foreign-body granulomatous reaction around the pigment, some of which appeared as crystalline masses. There were numerous multinucleated giant-cells, and some structures suggesting follicles. Most of the aggregates of pigment with their associated reticulo-endothelial reaction were in the region of lymph junctions alongside vessels or around atria a little distance beneath the pleural surface. There was a fairly marked increase in reticulin fibrils, but only slight collagenous fibrosis.

The histological picture is unlike that produced by similar injections of silica particles on the one hand, and very different from that produced by an artificial, almost pure carbon, graphite on the other.

Discussion

It has been too readily assumed that graphite led only to a benign form of pneumoconiosis. From the information now available it is possible to say that prolonged exposure to substantial concentrations of graphite dust can produce a pneumoconiosis which, in its advanced stages, may result in complete incapacity for work and can be responsible for death. As with other forms of occupational disease of the lungs, there is a marked variation in susceptibility: some men show gross radiological changes after twenty years' exposure while others show only slight changes after even longer exposure. A striking feature of many cases is the relatively small degree of physical incapacity in relation to the radiological findings, and it appears that this form of pneumoconiosis is often well tolerated until the very late stages of the disease. When increasing dyspnœa does lead to incapacity, the further progress seems to be rapid.

The radiological picture is not that of classical silicosis, as the accepted discrete nodulation is seldom seen at any stage. Nor is the histological picture typical of silicosis: nodules resembling those of classical silicosis may be found occasionally but more commonly the picture is one of pigment aggregates with linear or radial fibrosis and an accompanying focal emphysema. In advanced cases massive areas of fibrosis occur without definite nodular formation. In these areas of massive fibrosis necrosis may lead to cavitation. In the small series of workmen reviewed, tuberculosis does not appear to play an important role.

It is evident that graphite pneumoconiosis closely resembles that of coal workers (Cummins and Sladden, 1930; Hart and Aslett, 1942; Gough, 1947) both in its histology and in its radiographic appearances. In both graphite workers and coal workers the earliest radiographic signs are reticulation, while the advanced stages show diffuse opacities scattered over both lung fields with the occasional presence of large masses. In both groups of workers necrosis in the centre of a fibrous mass may lead to cavitation and melanoptysis (Dunner and Bagnall, 1946; Stewart and others, 1948) that usually occurs several years after leaving the causative employment: such cavities may not always be visible radiographically. Again in both groups of workers it is quite common to find fairly marked radiological changes in the lungs of men who have little disability. It is uncertain whether the curious bodies described in the lungs of coal workers by Tylecote and Dunn (1931) and by Williams (1934) are the same as the large irregularly rectangular masses of pigment seen in the lungs of graphite workers: they have many similar features.

Graphite pneumoconiosis, then, may be considered as an anthraco-silicosis similar to that of coal workers. For practical purposes graphite can be considered as crystalline carbon mixed with something of the order of 10 per cent. of free silica. It seems to us reasonable to assume that much of the damage to the lungs is produced by this silica, and that we are dealing with a form of silicosis modified by the presence of large amounts of other dust. It is possible also that the very large amounts of dust inhaled may themselves produce some change from sheer overloading of the defensive and drainage mechanisms of the lungs. It is, however, our impression, founded partly on animal work and partly on the examination of workmen, that a pure carbon artificial graphite does not lead to the changes described in this paper.

Conditions of work in the graphite industry vary enormously, and they have on the whole improved greatly in recent years. In view of the findings reported here, graphite can no longer be regarded as a harmless dust. The greatest amount of dust is evolved during the grinding of graphite, which should preferably be done in a totally enclosed mill with a mechanical feed and discharge: failing this, the installation of an adequate exhaust ventilation system is necessary. At all times exposure should be limited to that necessarily entailed in the feeding and discharge of the mill, and an efficient dust respirator is desirable whenever exposure to graphite dust is inevitable.

Summary

A brief description is given of the industrial uses of natural graphite, which is a crystalline carbon mixed with up to 10 per cent. of free silica and with other minerals. The greatest dust risk occurs in the grinding of natural graphite, and evidence is presented to show that this can lead to disabling and fatal pneumoconiosis. Marked changes in the lungs are, however, seldom seen in grinders who have less than twenty years' exposure. The results of three autopsies and some of the findings in other workmen are given, together with the results of some experiments on animals. The radiological and histological findings are similar to those found in South Wales coal workers.

We are grateful to Dr. N. T. Whitehead and Prof. P. L. Sutherland for their notes on the post-mortem findings in Cases 2 and 3 respectively, to Dr. J. C. Lees for the blocks of the lungs of Case 1, and to Dr. J. Glover for generous samples of graphite and carbon black. It gives us pleasure to record the helpfulness of Dr. A. I. G. McLaughlin and others in the Factory Department of the Ministry of Labour and National Service. The photographs were made by Mr. A. W. Collins, F.I.M.L.T.

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SICKNESS ABSENCE DUE TO PEPTIC ULCERS

BY

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According to an estimate made by Avery Jones and Pollak (1945), 1,500,000 men and women in England and Wales suffer from peptic ulcer, and Bockus (1943) expressed the general opinion when he said that " Well over 10 per cent. of all adults of the male sex have or have had an ulcer." It is therefore of considerable interest to determine the significance of peptic ulcer to industry, in terms of sickness absence.

During a survey undertaken to study occupational factors in the ætiology of peptic ulcer, it was possible to determine the sickness experience of a number of men with peptic ulcers and to compare it with the experience of men of the same age employed in the same occupation. All the men employed in a number of firms were interviewed by a social worker and particulars of their occupations were recorded, together with any symptoms of dyspepsia. Men who had had a peptic ulcer or who had symptoms of major dyspepsia were referred for a medical interview. They were accepted as having had a peptic ulcer only if a radiological or operative diagnosis had been made at hospital or if they had had a frank hæmatemesis; in addition, a small number were diagnosed radiologically in the course of the survey. Confirmation of the diagnosis was obtained directly from the hospital or doctor concerned in 77 per cent. of the cases, but when no medical evidence could be obtained (due to lack of records etc.) the men's statements were accepted. It is unlikely that this can have introduced much error as, when medical evidence was available, it conflicted with the men's statements in only 6 per cent. of the cases.

Method Adopted in the Present Study

The sickness absence of men with peptic ulcers was obtained from the firms' records for 1946 and, when the information was available at the time of the investigation, also for 1947.

Controls were chosen at random from the records of the survey from among men free from dyspepsia, of the same age, employed in the same occupation, and on the same type of shift. Whenever possible controls of exactly the same age were selected but, when they were not available, men whose age varied by four years or less from the corresponding ulcer cases were accepted. When no suitable control was available the ulcer case was omitted from the investigation. Altogether, records of 119 pairs were available, 96 for 1946, and 23 for both 1946 and 1947, making a total of 284 years' experience.

The material was collected from seven firms, six of which were in London while the other was in a small southern provincial town. The types of industry concerned and the occupations of the men are shown in Table 1.

The occupations of the controls were identical with those of the ulcer subjects and they have therefore been omitted from the Table. The recorded occupations are the occupations in which the subjects were employed at the time of the survey; changes in the course of the year have not been allowed for.

When a man was not employed by the firm for the whole year, an estimate of the annual absence was made from the experience of that part of the year for which he was employed. Little error can have been introduced by this as it applied to only 17 of the 284 man-years.

Findings

Sickness absence was measured in working days lost. The experience of the two groups of ulcer subjects and controls is summarized in Table 2.

From Table 2 it appears that when the subjects are divided into two groups, according to whether they had less or more than ten days' sickness a year, there is a significant difference between the ulcer subjects and the controls. This is confirmed when the sickness absence of each individual ulcer subject is compared directly with the sickness absence of the corresponding control. The results are shown in Table 3.

* Working with a grant from the Medical Research Council.

TABLE 1

OCCUPATIONAL DISTRIBUTION OF ULCER SUBJECTS

Social class	Occupation	Type of industry							Total number of men
		Electrical research laboratories	Civil Service	Dynamo manufacture	Glass manufacture	Goods transport	Passenger transport	Food preparation	
1 and 2	Professional	5	5	—	—	—	—	—	10
3	Foremen	—	—	—	—	2	2	—	4
,,	Electricians	—	—	2	—	—	—	—	2
,,	Mechanics and toolmakers	2	—	8	3	—	2	—	15
,,	Motor drivers	—	—	—	—	2	12	—	14
,,	Cooks	—	—	—	—	—	—	4	4
,,	Clerks and storemen ..	1	3	3	1	5	—	—	13
,,	Other skilled workers ..	1	—	—	—	—	1	—	2
4	Bus conductors	—	—	—	—	—	4	—	4
,,	Horse vehicle drivers ..	—	—	—	—	5	—	—	5
,,	Machine hands, semi-skilled	—	—	—	8	—	—	4	12
,,	Packers	—	—	1	2	—	—	1	4
5	Porters	—	—	—	—	12	—	—	12
,,	Messengers	—	7	—	—	—	—	—	7
,,	Labourers	—	—	1	4	—	3	3	11
	Total	9	15	15	18	26	24	12	119

From Table 3 it appears that the average sickness absence of men with proved peptic ulcers is 6·0 working days a year more than that of comparable controls without dyspepsia.

The excess sickness absence was practically the same whether the ulcer was gastric or duodenal and whether the man was under or over 45. The results are shown in Table 4 but, in view of the large size of the standard errors, it is not desired to attach much significance to them.

Discussion

In the seven firms included in the investigation a total of 155 proved ulcers were diagnosed among 2,871 men, giving an incidence of 5·4 per cent. A mean of 6·0 days' excess sickness absence in peptic ulcer subjects therefore indicated an annual absence of 32·4 working days per hundred men which could be attributed directly or indirectly to peptic ulcer. In addition, a number of men in whom the diagnosis

TABLE 2*

ANNUAL SICKNESS ABSENCE

Class of men	Number of Men							Working days lost	
	Working days lost								
	0—	1—	10—	20—	50+	0—	10+	Mean	Standard error
Ulcer subjects	39	43	26	21	13	82	60	16·37	2·17
Controls	47	52	21	17	5	99	43	10·32	1·55
	$\chi^2 = 6{\cdot}16$ $n = 4$ $10 < P < 0{\cdot}20$					$\chi^2 = 4{\cdot}40$ $n = 1$ $0{\cdot}02 < P < 0{\cdot}05$			

* The inclusion of the sickness absence of 23 men for two years, counting each year's experience as a separate observation, is open to theoretical statistical objections. For if a man's sickness absence in one year is correlated with his sickness absence in another, the observation of a second year's experience would not increase the statistical significance of the comparisons between men in the same way as would fresh observations in different men. In this instance the objection is not of practical importance as the correlations between the experiences of 1946 and 1947 are low;

Sickness absence of ulcer subjects, $r = 0{\cdot}076$
,, ,, ,, controls, $r = -0{\cdot}110$
Difference between sickness absence of ulcer subjects and controls, $r = 0{\cdot}083$
None of these correlation coefficients are significant ($P > 0{\cdot}05$).

TABLE 3*

DIFFERENCE BETWEEN SICKNESS ABSENCE OF ULCER SUBJECTS AND CONTROLS

No. of pairs (n + 1)	Total difference (days) S (x)	Mean difference (days) $\bar{x} = S(x)/n+1$	Sum of squares $S(x^2)$
142	859	6·05	158,273

Variance, σ^2, = 1085·6500 $t = \bar{x} \Big/ \frac{\sigma}{\sqrt{n+1}} = 2{\cdot}20$

Standard error of mean = 2·75 n=141, 0·02<P<0·05

* See footnote to Table 2.

was not proved had symptoms suggestive of peptic ulcer, so that the total sickness absence from this cause was probably appreciably greater.

The most closely comparable figures are provided by the Reports on Incapacitating Sickness issued by the Department of Health for Scotland. For the year 1936–37 these showed a loss of 33·3‡ working days per hundred men from peptic ulcer (Department of Health for Scotland, 1939). The Scottish figures are based on insurance certificates and are, therefore, not strictly comparable. It is probable that a proportion of the absence due to peptic ulcer is attributed to such general conditions as gastritis or dyspepsia. Nevertheless, the two figures are of the same order of magnitude and their similarity confirms the general validity of the findings.

This large amount of sickness due to one condition provides a serious challenge both to medicine and industry. It is evident that 5 per cent. of the male working population, who can make a substantial contribution to the national effort, cannot be excluded from ordinary employment, quite apart from the necessity of providing for the individual. Indeed, any attempt to eliminate peptic ulcer subjects from industry would result in a loss of a high proportion of the most valuable individuals, for the personality which appears to be associated with duodenal ulcer is that of the hard-working conscientious man who is particularly suited to positions of responsibility. In the industrial survey of which the above investigation formed part, it was found that duodenal ulcer was particularly common in managers and foremen (Doll and Avery Jones, to be published) and while this might, to some extent, be attributed to the special anxieties of their position, it is equally possible to explain the association on the basis of personality factors.

TABLE 4*

EFFECT OF SITE OF THE ULCER AND OF AGE

Type of ulcer	No. of men	Mean excess sickness absence compared with controls (days)	Standard error of mean (days)
Gastric†	47	5·7	6·58
Duodenal†	81	7·5	2·50
Age under 45	51	5·8	4·10
Age over 45	91	6·2	3·67

* See footnote to Table 2.

† The sum of the numbers of men with gastric and duodenal ulcers is less than 142 as the site of the ulcer was not known in a few instances.

‡ The actual figures are 38·8 days lost due to peptic ulcer. They have been reduced to working days lost by the subtraction of one-seventh.

The ultimate aim is the prevention of peptic ulcer, but this will remain Utopian until more is known of the cause of the condition. Until then, all that can be done is to minimize the effect of ulcers by early treatment and by creating conditions in industry which will enable the peptic ulcer subject to carry on efficiently. A possible means by which this may be done is the provision of dietetic facilities in industrial canteens (Avery Jones and Newell, 1947). When this has been done it has been greatly appreciated by the employees, and although no figures are available to determine the benefits accruing, the size of the ulcer problem justifies the trial of every practical method to reduce the social and individual disability.

Summary

The sickness absence of men with proved peptic ulcers has been compared with that of men without dyspepsia, of the same age, employed in the same occupation.

In seven firms, employing 2,871 men, the mean sickness absence of men with proved peptic ulcer was 6·0 working days a year (standard error 2·75 days) more than that of the controls.

The percentage of men who had proved peptic ulcers was 5·4, so that the total sickness absence attributable to peptic ulcer was 32·4 working days a year per hundred men.

Early treatment and the provision of dietetic facilities in industrial canteens are the most practical steps that can be taken to reduce this loss.

Our thanks are due to Dr. F. Avery Jones, to whose interest in the subject this paper owes its origin.

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BOOK REVIEWS

Basic Principles of Ventilation and Heating. By Thomas Bedford, D.Sc., Ph.D. 1948. London: H. K. Lewis and Co. Ltd. Pp. x+401. Price 25*s.* net.

This admirable book, well written by a recognized British authority, deals with "ventilation and heating in terms of basic human needs." It gives a full presentation of the fundamental physical and physiological principles involved in providing a comfortable thermal environment in the home and in the working place, and is intended to supplement the technical details of heating and ventilation practice found in standard works. The historical reviews of the research work, often extending over many years, leading to our present knowledge of comfort needs and their measurement, heat loss and gain from the human body and from buildings, heating and ventilating appliances, etc., form a valuable feature of the book. Dr. Bedford has himself made extensive contributions to several aspects of the subject.

Enough is known about the requirements for thermal comfort for it to be possible to assess an environment instrumentally and to define it in terms of the "effective temperature" (U.S.A.) or of the "corrected effective temperature" (Bedford). Not only must air temperature and humidity be taken into account, but also air movement and the effect of radiating surfaces. A sense of "freshness" must be maintained, not only by removing odours and atmospheric contaminants, but also by providing variable air-movement (but, of course, not enough to cause noticeable draughts). Adequate ventilation, suitably introduced and distributed, is an important consideration in providing suitable factory conditions. Most people feel comfortable within a narrow range of (corrected) effective temperature, the actual value depending on the extent of the activity and on the clothing being worn.

The necessity for understanding basic principles completely is clear from the following quotations:

> "In a fully occupied workroom some people must generally work near windows, and in cold weather they are liable to be exposed to unpleasant draughts. Even when the windows are closed, the warm air of the workroom coming into contact with the cold window surfaces is cooled and falls rapidly towards the floor. This descending current of air often provokes complaints of draughts" (p. 185).
>
> "It is therefore preferable to circulate a larger quantity of air at a moderate temperature rather than a small quantity at a high temperature" (p. 210).

We are all conscious of the poor standard of household heating in this country. Bedford describes modern methods and appliances and discusses the characteristics of the environment produced by both the new and old. Again, an understanding of the principles involved in providing thermal comfort would seem to be of importance when appliances are being designed and installed. The choice of building materials and the placing and design of windows, doors, etc., must be considered when striving for maximum efficiency.

The book is well produced and contains 123 illustrations and 345 references to the literature. Heating and ventilating engineers, industrial medical officers, and all interested in the many aspects of thermal comfort should find Bedford's book of great value. *H. H. W.*

Lehrbuch der Arbeitshygiene. By Franz Koelsch. Stuttgart: Ferdinand Enke Verlag. Vol. 1, 1947. Pp. 367. DM 29.50. Vol. 2, 1946. Pp. 483. DM 34.

Koelsch begins his first volume with an interesting historical introduction. He notes that Aristotle described diseases peculiar to couriers, the deformed ear of the boxer, and other occupational stigmata. In Germany the first publication dealing with industrial disorders appeared in 1473, when Ulrich Ellenbog of Augsburg wrote on poisonous vapours and smokes. He had observed the effects of these on metal workers who used gold, lead, and mercury. In later years Paracelsus, Ramazzini, and many other notable writers preceded the authorities of today.

It is suggested that accident proneness may be detected in school children and will accompany them through life. Other characteristics of mental and physical constitution may be noted in youth and may perhaps be of value, even at an early age, in judging suitability for work. The writer has also described the commonest disabilities and has noted the types of employment that cannot be undertaken with these. In discussing fatigue, Koelsch notes that it is harmful when the point of exhaustion is reached, which may occur in the young, in the ambitious, or in those anxious about supporting their families. Such fatigue may fall on part of the body only, which is an implied criticism of the working conditions demanding enquiry by the employer.

Working places should have roofs not under 3 metres in height, and 2 square metres and 10 cubic metres are the minimum needed for each worker, assuming not less than three air changes an hour.

Night work in general is condemned though certain occupational groups such as writers, type setters, artists, and those doing fine mechanical work may work better at night.

The chapters dealing with accidents and with various forms of industrial poisoning are well arranged, and there is a useful table of the common industrial solvents, in which boiling points and explosive concentrations are given. Some attention is given to the parasitic diseases occurring in industry. In 1900–20 more than 20,000 workers in the Ruhr were infected with ankylostomes, but an intensive campaign has almost eliminated the disease from this area.

An account of social insurance and of the law concerning employment in Germany is given at the end of the first volume.

In his second volume Koelsch considers in detail the hygiene of various occupations. He includes many which are rarely considered in English textbooks. Among these are gardening and viniculture, forestry,

hunting, and fishing, the music trades, clothing, the film industry, and all kinds of transport. He thinks that Bornholm disease is confined to certain regions, and that it is possibly of spirochætal origin and is perhaps contracted by drinking from open streams. Certain agricultural chemicals and insecticides are toxic, especially when inhaled, and protective masks are indicated when handling aniline oil, Ceresan, and sundry other products.

In many German industries the products are examined by means of *x* rays or radio-active substances. Regulations have been laid down to prevent injury to personnel by emanations, and the design of all plant is supervised.

The German industrial regulations accept Weil's disease as occupational when it occurs in those constructing water-ways. New regulations also control the construction of living places on river and canal craft as well as those relating to larger craft at sea.

G. C. P.

The History of Factory and Mine Hygiene. By Ludwig Teleky. 1948. Columbia University Press. London: Geoffrey Cumberlege. Pp. xvi plus 342. Price $4.50 or 25*s*.

Industrial hygiene is a department of medical study whose present importance and scope may blind one to the fact that a century ago it was almost non-existent. We may easily forget that compensation for occupational disease was instituted in England only in 1906, in France in 1919, and in the U.S.A. (practice varying from one State to another) from 1911 up to the present decade; the tree has had little time yet for vertical growth but the branches are spread wide indeed, and this is the justification for Dr. Teleky's publication of a "handbook" history at so early a stage.

The early chapters are devoted to panoramic description of the development of legislation in the important industrial countries, and of the forces and organizations concerned. The data collected and correlated are sufficiently comprehensive to be of real value for primary reference, and many interesting comparisons are made, for example, the tendency in America for organization of industrial hygiene to be planned by specialist teams directed jointly by employers' and workmen's organizations, with that in England, where the responsibility for the workman's health is vested in the State.

The section dealing with occupational disease and accident also contains in small compass a surprising amount of factual information on preventive measures and researches for their perfecting, and a valuable bibliography. A retrospect is given of the several problems connected with mining: dust control, explosions, injuries, nystagmus, etc.; and the fine work and promising results of the South African Miners' Phthisis Bureau are indicated, as are the reports of successive Royal Commissions in this country. It is stated that in the U.S.A. (again largely owing to lack of uniform legislation in different States, and to the hindrance of political considerations) legislative control is often much less effective than in Europe, and in some of the States accident and accident-mortality are much higher than here.

The final section comments on some selected tables of morbidity and mortality figures and correlates them with the progress of the study of industrial hygiene.

This book is well worth attention of the reader who would view *en plein* the growth of industrial health legislation, for despite its breadth it is nowise superficial.

L. W. H.

Radon: Its Technique and Use. By W. A. Jennings and S. Russ. 1948. John Murray. Pp. 225. Price 18*s*.

This book is an account of the properties, production and uses of radon and must contain almost all that anyone can wish to know about it in connexion with its use for medical purposes. The text is clear, and the illustrations by line drawings and diagrams and photographs are admirable. Useful tables of necessary constants are, of course, included. The story behind the work to which the book is a sequel is one of continued, painstaking, and hazardous work in developing and improving the technique of production of radon by technicians, under the guidance of a physicist whose reputation in the field of radiation in medical work is of the highest. They have improved the technique, but in the process those carrying out the work have suffered damage to their hands in the cause of scientific research and medical treatment. The book is a worthy tribute to the skill and patience of the workers and a fitting memorial to the occupational risks. It contains full practical details of the production of radon, deals adequately with the fundamentals, and discusses the medical uses with special reference to modern dosage methods and techniques which have been used in medical work. Specialization is always capable of leading its exponents into wide fields of knowledge and in this case it has been necessary to show an insight into many fields of scientific work. Recent developments in connexion with the production of radio-active isotopes have led to many new methods in industry, in addition to the use of radio-active substances for such things as making radiographs of castings, luminizing instrument dials, and dust extraction. The risks to the workers have been increased, so that it is imperative that all concerned with this type of work should understand its scope, limitations, and dangers. I believe that this book on radon would be interesting and useful to all so engaged. The authors and their technical assistants are to be congratulated.

F. E.

Transactions of the Ophthalmological Society of the United Kingdom, 1946: Volume 66. 1947. London: J. and A. Churchill. Pp. lv+691, illustrated. No price given.

The following are the most important contributions published in this volume:

At the Annual Congress: The presidential address by C. B. Goulden on "Johannes Evangelista Purkinje." A discussion on "Ocular disturbances of malnutrition," opened by Air Vice-Marshal Livingston and Harold Ridley. Malnutrition amblyopia was the main topic discussed. The Bowman lecture by Arnold Knapp on "The present state of the Intra-capsular Cataract Operation." The subject is exhaustively dealt with.

At the Oxford Congress: Discussion on "Amblyopia" opened by Jameson Evans, Dorothy Campbell, and Harold Ridley.

Among the shorter papers the following are of interest: "The nerve fibre pattern of the human retina," Ballantyne; "Traversing intra-ocular foreign bodies with retinal detachment," Michaelson; "Retinal vasculitis of the young," Loewenstein, Michaelson, and Hill; "Retinal venous changes in diabetes," Seymour Philps; "The intracapsular cataract extraction," Lopes de Andrade; "Stereoscopic vision in monocular aphakia," Letchworth; "The simple method of calculation of the optic system in the high anisometropia," Melanowski; "The more important pages from the history of Polish

Ophthalmology," Melanowski ; " The muco-cutaneous junction of the lid-margin and the distribution of the tear fluid," Eugene Wolff ; " Is tobacco amblyopia a deficiency disease ? " Schepens ; " Some recent developments in artificial eyes," Fincham ; " Two cases of exogenous tubercular conjunctivitis displaying Parinaud's conjunctivo-adenitis syndrome," Healy ; " Proliferation of the epithelium of the lens," Samuels ; " Detachment following inflammation," van Heuven ; " Four patients showing two types of hereditary cataract in one family," Lloyd Johnstone ; " The state of the retina in diabetes mellitus," Ballantyne ; " Partial thrombosis of central vein," MacRae ; " Resection and recession in treatment of squint," Marshall ; " Divergent strabismus," Duthie ; " Retinal vascular changes studied in bulk," Loewenstein ; " A binocular ophthalmoscope for the examination of detachments of the retina," Schepens ; " Binocular scotometry," Zade ; " Pituitary tumour : deep *x*-ray irradiation," J. H. Young ; " A case of osteopetrosis (Albers-Schonberg as described in 1904)," J. N. Wheeler ; " Conservation of the wounded eye, excluding retained foreign bodies," Goulding ; " The organization of army ophthalmology in India," Bridgeman ; " Lime burn of conjunctiva and cornea treated with amnioplastin graft," Lavery ; " Ocular and general manifestations resulting from the manufacture of sesquisulphide of phosphorus," Fahy and Lavery. *A. L.*

A Short History of Ophthalmology. By Arnold Sorsby. Second Edition. 1948. London : Staples Press Ltd. Pp. 103, with diagrams. Price 8*s.* 6*d.*

In an introductory chapter the author traces the science of ophthalmology from the Babylonian period of 2,000 B.C. through the Egyptian, Greek, Arabian, and dark-age periods, to the modern era of rapid advance which began in the seventeenth century. In the succeeding chapters the anatomy, physiology, and pathology of the eye, cataract, glaucoma, and therapeutics are followed over a similar course. There are further chapters on spectacles, the ophthalmoscope, and British ophthalmology.

In spite of the large amount of information condensed into ninety-one pages, the book is readable. It is sufficiently comprehensive to provide a working knowledge of the subject for the general reader and to form a framework for those whom it may stimulate to learn more. It has the added advantage of easily fitting a pocket. *A. L.*

BRITISH AND FOREIGN OFFICIAL PUBLICATIONS

Industrial Fluorosis. A Study of the Hazards to Man and Animals near Fort William, Scotland. By John N. Agate, G. H. Bell, G. F. Boddie, R. G. Bowler, Monamy Buckell, E. A. Cheeseman, T. H. J. Douglas, H. A. Druett, Jessie Garrad, Donald Hunter, K. M. A. Perry, J. D. Richardson, and J. B. de Weir. 1949. M.R.C. Memorandum No. 22. London : H.M. Stationery Office. Pp. viii+131. Illustrated. Price 4*s.*

The sequence of events which commonly leads to a detailed study of a hazard in industry begins with suspicion that a particular operation (or group of operations) bears a significant correlation to the incidence of pathological effects observed in the operators. It is probably very rare for the sequence to begin with unsought-for effects on animals. Inasmuch as animals are involved in routine toxicological studies, their contribution is usually to confirm the pathological effects or to offer facilities for the analysis of the disturbances brought about by the toxic product. There is, however, a sense in which animals should enter first in the sequence by yielding information on the materials involved, before adverse effects on workmen can result from exposure to them. Such an approach to industrial toxicology is not easy but is becoming more generally recognized. The traditional way of waiting until disease or death is reported among exposed workers is still too frequently adhered to.

This Report to the Fluorosis Committee deals with the results of four years' work on the hazard of fluorosis in an aluminium factory in Scotland, from the management and personnel of which no complaint of illness or poisoning had been made. A considerable literature existed on the toxic effects of fluorides which, whether exhibited in factories as dust and fume or in the water ingested by populations living in areas with high concentrations of fluorine, lead to striking changes in the skeleton, teeth, and ligaments. Had it not been for the fact that in 1943 and 1944 various crofters and farmers from the areas round the factory complained of a mysterious debility of their sheep and cattle, the present study of men and women in the factory might not have been undertaken. Although it is fair to say that the careful clinical and radiological observations on factory operatives and on inhabitants in the surrounding country did not bring to light marked or disabling degrees of fluorosis, sufficient deviation from normality was discovered to suggest that the earlier stages of the disease had already been reached in a high percentage of the workers.

The chemical hazards (gaseous and particulate fluorides) arising in the electrolytic separation of aluminium from alumina (Al_2O_3) dissolved in a bath of fused cryolite (Na_3AlF_6) may be divided into those arising from the electrolytic furnaces and discharged into the working room, and those discharged from the factory from the fume extraction plant. The latter appear as a cloud rising from the factory and, according to the wind prevailing, give rise to different patterns of concentrations in the atmosphere. The curves of concentration gradient from the furnace rooms in the factory to one mile into the surrounding country were more or less identical for

gaseous and particulate fluoride. The fall is steep, so that at two hundred yards from the factory the concentration is about 15 per cent. of the mean concentration in the furnace rooms, and at one mile it is only 3 per cent.

Many analyses were made of soil samples up to seven miles from the factory, at which distance to the north-east the fluorine concentration was still over four times the control values, the prevailing wind being south-west. At some three miles to the north-west the fluorine content was at control levels. Correspondingly the fluorine content of grass samples was highest in the north-east regions and this is, of course, the main source of excessive fluoride ingested by animals grazing in pastures round the factory area.

The high fluoride deposition on (and to a high degree penetration into) the pasture lands led to severe dental lesions and bone fragility in the animals, the former being established only in animals which had access to the fluoride contaminated pastures before their permanent teeth had formed. The bone dystrophy, however, occurred even in animals coming to the pastures late in development.

The dental changes, mottling, distortion, deformity of the incisors, and excessive wear of the cheek teeth led to selective abrasion so that the teeth developed long points and, by interlocking on opposing jaws, prevented the lateral grinding movements which are essential to the process of chewing the cud. The consequent chronic indigestion and distension of the rumen led to a form of starvation with debility and emaciation. Enormous quantities of fluorine were found in the teeth, mandibles, and ribs, the ratio to maximum normal values being from about 20 to 90. The investigators take the view that fluoride absorption is not in itself the cause of the debility and loss of weight, but that these arise from the failure of successful cud chewing due to dental disease, since mature animals put on the contaminated pastures remained unaffected.

Multiple fractures of ribs, mandible and pelvis in the affected animals were recorded. The assimilation of fluorine in some peculiar way leads to weakening of bones. Some evidence from animal experiments indicates that fluorine brings about disturbances in calcium and perhaps phosphorus balance; thus, bones of pigs fed on fluorine contained low calcium and high phosphorus: rats fed on fluorine retained much less calcium and rather less phosphorus, and excreted far more calcium in the fæces than did controls. Some evidence has also been obtained that an increased dietary calcium (0·23 per cent. raised to 0·73 per cent.) can diminish the assimilation of fluorine added to the diet: this effect is especially noticeable in the teeth and soft tissues. A fivefold increase of dietary phosphorus had no such effect when calcium was maintained constant.

Whilst a great deal has been reported on the pathological effects of fluorine in both man and animals, it is still far from clear why the fluorine becomes deposited in bones and teeth, how calcifications take place in ligaments, and what stimulates the formation of exostoses.

In Part V of the Report to the Fluorosis Committee very interesting measurements are given of the strength of bones (breaking stress, bending moment, and modulus of elasticity), taken from fluorotic and control animals. Strong evidence is given of a relation between the reduction in breaking stress and fluorine content of bone. The bending moment remains high until the bones contain very high fluoride: the breaking stress, however, falls steadily with rise in fluoride. Since the breaking stress α bending moment/δ^3, where δ = smallest external diameter, it is reasonable to suppose that as the fluoride content rises there is some "compensating" increase in the transverse linear dimensions of the bone. Such an alteration of the bone would be useful in balancing the loss of strength and exostoses could, as the authors say, be regarded as a local over-activity of this process. Although teleology is not the heresy it used to be, one should be cautious in using such terms for a process which must in the last analysis surely be chemico-physical, it being merely fortunate that the fundamental properties of bone permit a "compensation" to be established. Teeth cannot "compensate," and so the animal finds little comfort in the teleology of bone.

The team handling the clinical and radiological side of the investigation soon met the stupidity (from which none of us can claim full immunity) which is the heart-break of every mass investigator. Many refused to co-operate at all, and many of those who did co-operate dropped out as the investigation proceeded. Various subterfuges had, therefore, to be employed to make even the elementary statistics collected yield comprehensible conclusions. There could be no doubt that the workers in the less modern furnace rooms inhaled a good deal of fluoride and correspondingly had a high urinary excretion of fluoride. Some of the older men who had been exposed to high concentrations of factory fumes for many years showed gross radiological abnormalities of the accepted fluorosis type. But the authors are cautious about minor degrees of abnormality and prefer to group them as abnormal *x*-ray appearances and to seek correlations with them. It was then found that of the furnace workers 25 per cent., of the general factory workers 8·3 per cent., of the local residents 4 per cent., and of the local school children 0 per cent. of those *x*-rayed showed abnormalities. *No case of clinical disability was found,* but the investigators consider that the *x*-ray findings are a sufficient warning of developments likely to come. Considering, however, that they radiographed thirty-three men of ages 30 to over 50 who had been fully exposed in the furnace rooms for a mean time of twenty-four years and of whom 66·7 per cent. (misprinted twenty-three years and 33·3 per cent. in Report, Table XXXVIII) showed abnormalities but no clinical disabilities, the outlook for the other workers does not seem too gloomy.

"Within the factory there was very little evidence of organic disease of a general nature and still less of abnormal physical signs which could be attributed to occupation. The same high standard of fitness was seen also in the residents from the surrounding district."

A careful dental examination of a large number of adults and children living in the areas round the factory revealed no abnormalities among the adults and, although 5·6 per cent. of the children showed mottled teeth, this figure did not differ sufficiently from that found in other areas to make it significant. Among the workers in the factory the dental findings did not suggest any effects of fluorine.

There is some feeling of anticlimax in this Report, a happy anticlimax in that the serious disabilities which could reasonably have been expected among the workers were not, in fact, found. The authors' conclusions are mild, and they go no further than to admonish people to keep themselves and their animals away from the contamination and to recommend the factory management to reduce the amount of fluorine to which their workers are exposed.

An uncritical review of the literature and a description of the analytical method for the determination of small quantities of fluorine are appended to the Report.

M. W. Goldblatt.

ABSTRACTS

(This section of the JOURNAL *is published in collaboration with the two abstracting Journals, Abstracts of World Medicine, and Abstracts of World Surgery, Obstetrics, and Gynæcology, published by the British Medical Association. The abstracts are divided into the following sections: toxicology; industrial physiology; industrial lung disease; industrial dermatitis; accidents and orthopædic surgery; industrial ophthalmology; environment; general. Not all sections will necessarily be represented in any one issue.)*

TOXICOLOGY

Effects of BAL and BAL Glucoside in Acute Lead Acetate Poisoning. WEATHERALL, M. (1948). *Brit. J. Pharmacol.*, **3**, 137.

Preliminary experiments with mice poisoned by daily intraperitoneal doses of 50 mg. of lead acetate per kilo showed that daily intramuscular injections of 20 mg. of BAL (2 : 3-dimercaptopropanol) per kilo or 1,000 mg. of BAL glucoside per kilo reduced the mortality. Mice were insensitive to oral doses of lead, and rabbits were therefore used for the study of blood changes. The fragility of washed heparinized rabbit erythrocytes in salt solutions was determined by plotting the probit of the percentage hæmolysis against the logarithm of the salt concentration. The concentration causing 50% lysis (LyC 50) was thus determined. The mean value of 54 observations on 22 normal rabbits was 0·51% of sodium chloride. Previous exposure of the cells *in vitro* to a solution of lead acetate containing 9 μg. of lead per millilitre increased the resistance of the cells, the LyC 50 being reduced to 0·35%; the slope of the fragility curve was less steep than the normal. Exposure in lead solution to which BAL (22·7 μg. per ml.) was added from the beginning gave a LyC 50 of 0·48%—a figure identical with that found with BAL alone. Four mols of BAL or BAL glucoside were thus sufficient to protect the cells against the action of 1 mol of lead. If the lead was allowed to act for half an hour before adding BAL the change was arrested, but there was no reversal of the change already established, unlike the action of BAL in reversing the poisoning of tissues with arsenic. Rabbit plasma also inhibited the action of lead upon erythrocytes, but when BAL was also present the protective action was less than with either substance alone. Also, plasma from rabbits previously treated with intramuscular injections of BAL in nut oil or propylene glycol was less protective than normal plasma. This change was unaccompanied by any alteration in plasma phosphate.

Rabbits given single oral doses of 300 mg. of lead acetate per kilo showed anæmia, punctate basophilia, and a reticulocyte response, together with hæmoglobinuria, slight albuminuria, and an increased excretion of coproporphyrin. The slope of the red-cell-fragility curve was flattened, especially in rabbits with severe anæmia, but there was no significant change in LyC 50. Hæmoglobin (but no red cells) was present in the urine for 2 or 3 days; the daily urinary coproporphyrin excretion was increased to about 45 μg. per day and remained above the normal (about 5 μg. per day) for at least 3 weeks. BAL given alone had no effect on the blood, but increased the coproporphyrin excretion to 12 to 20 μg. per day. In rabbits poisoned with lead and then given intramuscular injections of 50 mg. of BAL per kilo 1 hour later and 25 mg. per kilo subsequently at 8-hourly intervals for 2 days, the anæmia and reticulocytosis were reduced and did not appear while BAL was present in the blood stream. The urinary coproporphyrin was increased to about 90 μg. per day—a figure greater than that expected from simple addition of the effects of lead and BAL. Fæcal coproporphyrin was slightly increased. The effects of BAL glucoside were similar but less marked, possibly because of more rapid excretion of the more soluble compound. The mortality of the animals was unchanged by BAL but was prevented by BAL glucoside. The number of animals used was too small for the differences in mortality to be significant.

Attention is drawn to the similarities between the action of BAL and BAL glucoside in lead and in cadmium poisoning. The results do not warrant the use of BAL in chronic plumbism in man, but it is considered that it is premature to reject all dithiols as useless or dangerous for this purpose.

[At all points in this careful work the conclusions are backed by control experiments and statistical evidence.]

L. G. Goodwin.

Sodium Pyrocatechindisulphonate and Urinary Excretion of Lead in Experimental Poisoning. (Pirocatechindisulfonato di sodio ed eliminazione urinaria del piombo nella intossicazione sperimentale.) BORGHERO, A. (1948). *Med. d. Lavoro*, **39**, 146.

The author had previously described the effects on porphyrinuria in rabbits when sodium pyrocatechindisulphonate was injected intravenously at the same time as lead nitrate. In the experiments now described the elimination of lead was observed during a course of these injections. To begin with, 5 animals were injected with lead alone, and all died within 23 days. The urinary excretion of lead was high throughout and tending to rise. A second series of 5 animals received lead and sodium pyrocatechindisulphonate, and, though their urinary lead excretion fell below that seen in the first series only 1 animal died, from intercurrent disease.

It is possible that the sodium salt was given in inadequate amount, and that the lead excreted in the urine had not reacted with it but represented the excess. A surprising observation was the rapid fall in urinary lead when injections ceased. The author suggests that the pyrocatechindisulphonate may cause lead to be excreted by the bowel or fixed in the tissues in an innocuous form. Other substances used to treat lead poisoning cause a more lengthy excretion. The pyrocatechindisulphonate reduces the urinary lead by about two-thirds.

G. C. Pether.

The Penetration of Lead Through the Skin. LAUG, E. P., and KUNZE, F. M. (1948). *J. industr. Hyg.*, **30**, 256.

The authors found that the kidney and certain other tissues serve as " biological magnifiers " in concentrating minute quantities of lead which entered the organism. Rats were employed in the tests.

Kehoe's experiments indicated that lead tetraethyl readily penetrates the skin, frequently with fatal results. The authors confirmed that finding. In their tests they took special precautions to prevent inhalation of the volatile lead tetraethyl by the rats, and they found that after the application of 105 mg. of lead (in the form of tetraethyl) to 5 rats, their kidneys and livers contained 42 to 92 μg. of lead, and the lung tissue not much less. Even the muscle and brain contained 8 to 22 μg.

Study of Lead Exposures in Three Metropolitan Newspaper Plants. KEPPLER, J. F., and BUMSTED, H. E. (1948). *Occup. Med.*, **5**, 65.

The lead content of the atmosphere and of the workers' urine was estimated to test the claims of the labour unions that there were cases of lead-poisoning in certain printing-works. Linotype operators were not exposed to a significant lead hazard : their average excretion was 0·028 mg. per litre, and the average atmospheric lead concentration at mouth level was 0·035 mg. per cubic metre. Such atmospheric lead as was present came not from the melting-pots but from the sawing of the " slugs." The sawing process in other departments could give rise to a lead hazard. There was also danger intermittently near the re-melting pots, and in the stereotype departments during the " drossing " of the pots and blowing off dust with air hoses. Nevertheless, the average lead excretion of stereotypers was within normal limits, and only 21% of them excreted more than 0·1 mg. per litre of urine. There was a significantly higher excretion among stereotypers than among linotype or other workers.

The authors conclude that all re-melting and stereotype casting-machine pots, drossing processes, and all saws and trimmers should have local exhaust ventilation. The use of air hoses for blowing off dust should be discouraged. *J. N. Agate.*

Protection against Radiation Hazards and Maximum Allowable Exposure Values. MORGAN, K. Z. (1948). *J. industr. Hyg.*, **30**, 286.

Because of the unprecedented precautions taken in America in the plutonium projects, not one of the thousands employed during the last 5½ years has received any radiation damage. One of the most important contributing factors to this safety record was the creation, in 1942, of the Health Physics Division, composed of physicists, chemists, and engineers. They adopted a value of 0·1 r per day as a tolerance dose, and it seems that this rate of exposure may be continued for a number of years without causing perceptible biological damage. However, experiments by Lorenz on mice indicated that levels as low as 0·11 r per day might cause a decrease in their life span, and might induce ovarian tumours. He suggested in 1946 that the permissible dose for women exposed to radiation for many years should be limited to 0·02 r per 8-hour day. Sievert, in 1947, thought it advisable to fix the safety tolerance dose for general radiation at 0·01 r per day.

The precautions taken to reduce the radiation exposure in plutonium projects consist of concrete walls 6 ft. (1·8 m.) in thickness built round the pile. Radiating objects are withdrawn from the pile with long rods, and the objects are pushed into lead coffins or dropped into a deep water canal. Chemical operations on radioactive materials are done behind shields, and all manipulations are performed by remote control. A monitron is continuously in operation, and it sounds an alarm when the radiation exceeds 0·1 r per 8 hours.

H. M. Vernon.

Radiation Hazards in Industry. WILLIAMS, C. R. (1948). *J. industr. Hyg.*, **30**, 294.

Most industrial *x*-ray units are operated at voltages below 400 kV. High-voltage *x*-ray equipment (1,000,000 and above), because of extreme penetrating power, is used in industries making large castings, pressure vessels, and the like. Most installations are in completely enclosed areas having thick concrete walls, but the low-voltage units are often not adequately shielded.

Shoe-fitting fluoroscopes have been used for several years for fitting shoes. The units usually consist of a 50-kV. *x*-ray tube, housed in a lead-lined case having an opening for the customer to place his feet, and three viewing openings. Values ranging from 0·5 to 5·8 r per second have been observed, so that in a 20-second exposure it is possible to deliver more than 100 r to a foot. Leakages from the cabinet may affect persons near by, though the total exposure does not usually reach 0·1 r each day.

Anti-theft fluoroscopes have been designed to combat theft of tools and parts from industrial plants. Usually only 1 person in 25 or 30 is subjected to fluoroscopy each day, the average whole-body exposure being about 0·2 r per inspection.

In the radiography of castings and pressure vessels the radio-active source is radium sulphate enclosed in a hermetically sealed silver capsule. The most common sources contain 100 to 200 mg., and the greatest problem comes from handling the source by unauthorized persons who are ignorant of its nature. Extraordinary precautions should be exercised at all times.

Linear sources of radio-active material have been applied successfully to the control of static electricity in textile and other industries. The quantity of static electricity removed depends on the intensity of the alpha-radiation. The radium source (ionotron) consists of a thin metallic foil with a radium salt incorporated in it. The foil is placed in an aluminium housing, and the beta- and gamma-radiation given off at the same time as the alpha-radiation is dangerous, requiring adequate protection for the workers. Self-luminous paints produce fluorescence when mixed with a phosphor such as zinc cadmium sulphide. They are much employed for painting dials of watches and other instruments. During 1940 several thousand persons were employed in the industry in the U.S.A. Adequate protection is necessary.

H. M. Vernon.

Inability of 2–3 Dithiopropanol (BAL) to Protect the Liver Against Toxic Action of Uranium Nitrate. MACNIDER, W. DEB. (1948). *Proc. Soc. exp. Biol., N.Y.*, **68**, 160.

The author has shown that doses of BAL (10%, benzyl benzoate 20%, in peanut oil) equivalent to 15 mg. per kilo, when administered subcutaneously to dogs for 8 days, were ineffective against the hepatatoxic action of 4 mg. per kilo of uranium nitrate ; rather it tended to increase the toxic effects. The livers showed diffuse necrosis with advanced fatty degeneration.

G. F. Somers.

The Pathogenesis of the Liver Lesion Due to the Administration of Carbon Tetrachloride. ANDREWS, W. H. H., and MAEGRAITH, B. G. (1948). *Ann. trop. Med. Parasit.*, **42**, 95.

Subcutaneous doses of carbon tetrachloride (0·1 g. per 100 g. body weight) induce centrilobular degeneration and necrosis in the livers of animals. Swelling of the parenchymal cells is a fairly early, though variable, feature and, in the opinion of the authors, leads to obstruction of the flow of blood through the sinusoids with centrilobular anoxia. [Most of the conclusions are based upon rat experiments in which swelling of liver cells is pronounced; the authors admit that sinusoids are usually not obliterated in the guinea-pig, yet necrosis may be severe.] *G. R. Cameron.*

Pathology of Carbon Bisulphide. (Sulla patologia da solfuro di carbonio.) GRAZIANI, G., and PECORA, L. (1948). *Folia med., Napoli.*, **31**, 129.

Carbon bisulphide intoxication is one of the best studied of industrial hazards and precautions have made it a rarity. Nevertheless, these authors, investigating 17 males, aged between 22 and 58, who worked for 1 to 15 years on extracting oil with carbon bisulphide from olive pulp, believe that they have detected a subclinical intoxication with 0·006 to 0·012 mg. per litre. Various authors have given the maximal safe concentration as between 0·03 and 0·1 mg. per litre; toxic reactions, mainly in the central nervous system, have been attributed to long exposure to concentrations usually thought safe. Arguing that nervous function depends on rapid destruction of acetylcholine by cholinesterase—many think that carbon bisulphide disturbs cholinergic functions—they adduce as evidence of subclinical intoxication the consistent finding of a high cholinesterase and a low vitamin B_1 level in the subjects' blood. Clinical evidence of "vegetative dystonia" is alleged from electrocardiographic changes—a triphasic rapid wave—of debatable significance, and a prevalent bradycardia (*sic*) of about 60 a minute. *John Hambling.*

Field Tests for the Detection of Carbon Monoxide. MINCHIN, L. T. (1948). *Chem. and Ind.*, **67**, 147.

The author refers to the laboratory method of estimating CO by the reaction with iodine pentoxide. Unless frequently calibrated this may give very misleading results. One such method involves the use of the pentoxide in a mixture with sulphuric acid. Sealed tubes are broken before use and the suspect vapour is drawn through them by a pump. Even this method is rather insensitive.

It is desirable that any apparatus used should be small and easily portable. A catalytic mixture of copper, manganese, cobalt and silver oxides will convert CO to CO_2 and the heat evolved may be measured, but an instrument based on this principle also requires constant checking. Several kinds of apparatus based on this reaction are available.

Methods based on the reduction of palladous salts have also been employed for some years and a simple device of this kind has been used by the Post Office for some time. It is not always convenient, as no means are provided for testing a sample of air removed from a distant site. It is also not specific for CO and will react with H_2S. Modifications of the Post Office method involve the use of palladium chloride in a solution of acetone.

During the war developments in the use of palladium salts were stimulated by the necessity of detecting leakage of CO into the interior of aircraft. The British apparatus consisted of a container of silica gel impregnated with potassium pallado-sulphite. Suspect gases are passed through a column of plain silica gel which removes interfering substances and then enter the palladium sulphite column in which a colour change indicates the presence and concentration of CO.

An apparatus based on this principle is now available and will give an indication of 0·003% CO in two minutes and approximate estimates between this figure and 0·04% in the same time.

Minchin has perfected an instrument which is most convenient for utilizing the tubes employed in the method just described. It is compact and easily carried and enables a steady stream of air to be drawn through the CO test tube at the prescribed rate of 60 ml./min. The instrument has an indicator which shows the duration of the test. The method is specific for carbon monoxide except that H_2S or PH_3 may interfere. These can be removed by a silica gel tube saturated with silver acetate.

The aspiration is effected by the flow of a known volume of water at a constant rate. This runs from the upper to a lower chamber. The same water may be used repeatedly by returning it to the upper chamber after each test by inverting the apparatus. Though designed primarily for testing CO, the apparatus may evidently be used for other gases for which colour tests are used. By turning off the tap at any stage one may estimate the amount of gas which has entered by reading the gauge. If so desired a palladium chloride test paper may be used instead of the silica gel tube.

It is evident that by using a sufficient length of tubing the suspect vapour may be extracted from a point which is otherwise inaccessible.

G. C. Pether.

A Study of Resuscitation from the Juxtalethal Effects of Exposure to Carbon Monoxide. SCHWERMA, H., IVY, A. C., FRIEDMAN, H., and BROSSE, E. LA (1948). *Occup. Med.*, **5**, 24.

In this experiment 310 dogs were exposed in a chamber to a mixture of air and coal gas with a carbon-monoxide concentration of 0·3%. To determine the course of the intoxication 52 animals were exposed till they died. The remainder were removed at the first respiratory gasp, and either not treated or given artificial respiration manually or mechanically. The mean survival time for the 52 controls was 39·9 minutes, and the mean survival time after the first gasp, 3·8 minutes. It is shown that the first gasp is a reliable point at which to begin resuscitation experiments. Of 22 dogs given no resuscitation 8 survived; of 20 given simple artificial respiration in air 10 survived, but the difference is not statistically significant. After simple artificial respiration with carbon dioxide in oxygen 13 out of 30 survived. Three mechanical methods of resuscitation—an alternating positive- and negative-pressure system with pure oxygen, the same device with 7% carbon dioxide in oxygen, and an alternating positive-pressure device with pure oxygen—gave survival rates of 69%, 66%, and 65% respectively. For immediate survival the admixture of carbon dioxide seemed to make no difference. When the dogs had no palpable cardiac impulse on removal from the chamber, only 10 out of 69 survived. Contrary to expectation, the length of exposure to carbon monoxide did not appear to influence the chance of immediate survival.

In all there were 156 survivors; after a symptom-free interval of 2 to 12 days, 68 of them exhibited neurological sequelæ—apathy, tremors, ataxia, spasticity, or maniacal

restlessness. The incidence of sequelæ depended on the duration of the anoxia, but thereafter the incidence and severity were the same whether 100% oxygen or 7% carbon dioxide in oxygen was used in resuscitation. In 18 cases the neurological signs disappeared again in 3 to 11 days, and these animals had had relatively short exposures. Pneumonia also occurred as a sequel, but could not be definitely attributed to any one method of resuscitation. The use of 7% carbon dioxide in oxygen assists clearance of carbon monoxide from the blood, but affects neither survival nor the incidence of sequelæ. Necropsies showed that the immediate deaths were due to cardiovascular failure, and the authors consider that, in dogs, the state of the heart at the time when resuscitation is started is more important than that of the respiratory centre.

A historical review of treatment for carbon-monoxide asphyxia is given. *J. N. Agate.*

A Comparison of the Sensitivity of Methods Used for the Detection of Carbon Monoxide in Blood. WIKOFF, H. L., and CARSON, G. B. (1948). *Amer. J. clin. Path.*, **18**, 548.

The authors investigated the sensitivity of various methods for detecting carbon monoxide in blood. They concluded that ordinary spectroscopic methods fail if the saturation is less than 30%; with the Hartridge reversion spectroscope the sensitivity of the test is increased so that a saturation of 10% can be detected. With pyrotannic acid and with Wetzel's reagent (1% tannic acid) concentrations as low as 2% may be detected. Other tests, such as Liebmann's (formaldehyde), Haldane's (carmine dilution), Rubner's (basic lead acetate), and Katayama's (ammonium sulphide and acetic acid), are less delicate. *O. L. V. de Wesselow.*

Studies on Experimental Phosgene Poisoning. V. Infusions in the Treatment of Experimental Phosgene Poisoning. BRUNER, H. D., GIBBON, M. H., MCCARTHY, M. D., BOCHE, R. D., TALBOT, T. R., LOCKWOOD, J. S., and SANDERS, G. B. (1948). *Ann. intern. Med.*, **28**, 1125.

In phosgene poisoning the transudation of plasma into the pulmonary alveoli leads to two functional derangements, either of which is potentially lethal. One is the obstruction to pulmonary gaseous exchange due to the physical presence of this fluid in the alveoli and eventually in the bronchioles; the development and magnitude of this lesion can be evaluated by observing the arterial oxygen saturation. The second is loss of circulating plasma volume which results in a state very similar to secondary or surgical shock. On the whole, as is very clearly pointed out in the present paper, attempts to control the hæmoconcentration and to restore the plasma volume by infusions sometimes aggravate the double lesion either temporarily or fatally.

G. F. Walker.

Ethylene Glycol Poisoning. A Clinical and Pathological Study of Three Cases. HAGEMANN, P. O., and CHIFFELLE, T. R. (1948). *J. Lab. clin. Med.*, **33**, 573.

Three cases of fatal poisoning with ethylene glycol are described. All were characterized by coma, acidosis, convulsions, and death within 24 hours of drinking ethylene glycol. (The actual quantities drunk were not determinable.) The primary lesion in these cases was widespread capillary damage. Hæmorrhages in pleura, lung, heart, pericardium, kidney, and brain were found. Oedema and fatty infiltration were present in the liver, and calcium oxalate crystals were found in the kidney tubules and brain. Ethylene glycol was widely distributed in the body tissues and urine (the analytical technique is described in detail). Formaldehyde was also detected in small quantities in the urine. It is not clear whether death results from chemical meningitis or oxalate poisoning. The authors feel that oxalate formation is comparatively unimportant in these cases. Treatment was unavailing. Measures tried included gastric lavage and liberal administration of alkalis and fluids, sodium lactate, magnesium sulphate (for convulsions), and oxygen. *T. E. Graham.*

Methyl Bromide Poisoning. (L'intoxication par le bromure de méthyle.) DECHAUME, J., BOURRAT, L., SCHOTT, B., and BUFFARD, —. (1948). *J. Méd. Lyon*, **29**, 297.

A study of six cases of methyl bromide poisoning suggests that the poison takes particular effect on the upper cerebellar peduncles, the red and dentate nuclei, and the corpus striatum. The odour is not strong, so that inhalation may occur without the victim's knowledge. Symptoms may develop from 1 month to 7 months after exposure has ceased, but more acute illness may develop within 2 days. Prodromal symptoms are headache, nausea, vertigo, tremors, and painful hyperacusis. Dysarthria occurs with distortion of the peri-buccal musculature. In graver cases the cerebellar and labyrinthine symptoms are more evident. There may be somnolence, confusion, or coma or depression. Motor symptoms are rare, the pyramidal cortex generally escaping. There may be tremors and myoclonic movements. Some of the recorded cases resembled Kojevnikov's syndrome (epilepsia partialis continua). The later the onset of symptoms, the less acute the course and the better the chance of recovery. Symptoms may persist for from 12 to 15 months. Death is generally confined to acute cases.

Although adrenaline is suggested in treatment to lessen cerebral capillary vasodilatation, it does not seem to be of much benefit. The intractable myoclonias present a problem, though hyoscine therapy is said by some to be valuable. Prophylaxis lies in strict control in the construction and manipulation of apparatus.

G. C. Pether.

Poisoning by Sodium Chlorate. (L'intoxication par le chlorate de sodium.) DÉROT, M., DÉROBERT, L., GIRARD, M., DUPEYRON, T., and MENAGER, M. J. (1948). *Sem. Hôp. Paris*, **24**, 719.

Observations on 9 cases of sodium chlorate poisoning seen by the authors, and 1 other, are described. This salt had been taken by the patients in mistake for ordinary table salt, or had been dispensed for them in error in place of sodium sulphate. The course of the poisoning varied from a fulminating one, fatal in 10 hours, to a mild one with recovery. The fatal dose is estimated at about 30 g. Nausea, vomiting, severe cyanosis, and collapse were the immediate symptoms; oliguria and hæmoglobinuria appeared in 8 to 12 hours, and jaundice due to hæmolysis on the second day; death in coma occurred in the fatal cases in 8 to 48 hours. Differential diagnosis is from other types of hæmolytic poisoning, such as by *Clostridium perfringens* infection, arsine, dinitrobenzene, aniline, and nitrites. Proof is obtained by a history of ingestion and/or by chemical tests for chlorates in the urine. Post-mortem examination revealed parenchymatous degeneration of the liver and

of the kidney, which contained much pigment in the tubules. The cyanosis is due to methæmoglobin, and the authors discuss the biochemical reactions by which this is caused. *H. K. Goadby.*

Hæmorrhagic Syndrome due to Benzene with Simple Morphological Platelet Changes. Value of Systematic Platelet Examination in Workers Exposed to Benzene. (Syndrome hémorragique benzolique avec simple altération morphologique des plaquettes. De l'utilité d'examen systématique des plaquettes sur lame chez les ouvriers exposés au benzol.) FAVRE GILLY, —., MOREL, —., and BRUEL, —. (1948). *Arch. Mal. prof.*, 9, 274.

A man, aged 47 years, engaged in making laminated sheets of rhodium alloy, where he was exposed to benzene vapour for 13 years, complained of weakness and nose bleeding. Three years previously, because of complaints of nose bleeding and the consequent discovery that the erythrocyte count had fallen to 3,800,000 per c.mm., he was temporarily removed from exposure to benzene. He was admitted to hospital because he developed vertigo of the labyrinth type (later considered to be due to hæmorrhage). Clinical examination revealed little abnormal (except that partial colour blindness to red, blue, and green suggested a retrobulbar neuritis). The red cell and white cell counts were within normal limits but a slight neutropenia was present. The platelet count was normal, but the platelets showed morphological abnormalities (including a predominance of large oval platelets with numerous granules) and a tendency to agglutinate. The coagulation time was prolonged.

The authors suggest that with adequate hæmatological control, necessary because similar changes in platelets may occur in women during menstruation, the alteration in the platelets may be a simple test in the medical supervision of workers exposed to benzene vapour.
T. A. Lloyd-Davies.

Three Cases of Mercurial Tremor Treated with Sodium Thiomalate. (Trois cas de tremblement mercuriel. Effects du traitement par le thiomalate de soude.) WORMS, R., WEILL-HEULOT, —., and TUBIANA, M. (1948). *Bull. Soc. méd. Hôp. Paris*, 64, 478.

The 3 patients described were all electricians who made mercury interruptors. The first, aged 63, had been working for several years with mercury when an acute generalized tremor started in 1940; it interfered with the precision needed for his work. With rest it disappeared, but reappeared at intervals, and in January, 1948, he was considered to have Parkinson's disease. He could neither write nor walk, and had a rapid fine tremor, worst in the extremities; his face was wasted and pale. His speech was monotonous, nasal, and explosive in character, and there was an intention tremor made worse by emotional upsets. There was a childishness about his behaviour, and an indifference to circumstances. He also had an external strabismus and considerable dysmetria. After treatment with atropine (61 mg. subcutaneously in 3 weeks) there was great improvement; he could walk and write again, but his voice remained the same. He gained 5 kg. in weight during 1 month.

The other 2 patients were treated with sodium thiomalate. Their histories and symptoms were much the same as in the first case. The third patient had worked since 1920, his tremor first appearing in 1941, and becoming much less when he was on holiday in the summer. Both had moderate microcytic anæmia. Each received the same treatment, 1·0 g. of sodium thiomalate injected 6 times daily for 3 days. On the second day there was great improvement, and after the course was over both could perform complicated actions with their fingers, such as buttoning their coat, and vision was normal; appetite improved, and they put on weight rapidly. After 2 weeks improvement was maintained in 1, but the other, 3 days after the course, developed flexor spasm of the left arm and wrist, followed by slow regular involuntary movements; hypertonus appeared if the arm was passively flexed several times.

The authors consider that there were 3 conditions in these cases; as well as the mercurial tremor, there was a cerebellar syndrome (characterized by intention tremor, scanning speech, dysmetria, and a diadochokinesis) and an extrapyramidal syndrome (Parkinsonian tremor at rest, rigidity, increased postural reflexes). They consider that the term "mercurial encephalopathy" might cover the complex of syndromes. The mercury is oxidized when in contact with the air, and can thus enter the body through the lungs and through the gut (fingers to mouth); moreover, symptoms are liable to recur years after ingestion, following an attack of influenza or some other illness (with reappearance of mercury in the urine), because the heavy metal associates with the protein in the cells. Dimercaptopropanol (BAL) has been used against mercury because of its power of dissociating this union, but the authors recommend sodium thiomalate because it is 20 times less toxic than BAL (the respective lethal doses in the mouse being 0·15 g. per kg. for BAL, and 3 to 4 g. per kg. for thiomalate). They thus consider that the arm signs in the third patient after treatment were not due to an overdose, but to liberated mercury reaching a centre in the cerebellum. This has happened when workers in mercury and arsenic have been treated with BAL. *T. E. C. Early.*

Hair Loss in Neoprene Manufacture. RITTER, W. L., and CARTER, A. S. (1948). *J. industr. Hyg.*, 30, 192.

Loss of hair has been noticed among employees engaged in manufacturing one of the synthetic rubbers, and the authors have attempted to isolate the substances responsible for the loss. Synthetic rubbers are products obtained by the polymerization of certain unsaturated compounds. Neoprene is the generic name of the class of elastomers produced by the polymerization of 2-chlorobutadiene ($H_2C=CCl-CH=CH_2$). This substance—a colourless liquid—is formed from acetylene and hydrochloric acid by a series of reactions. Because of the hazardous nature of the reactions they are carried out in a closed system. Chlorobutadiene is polymerized after initiation by means of typical catalysts of the persalt type, a sulphur-containing compound of the thiuram type being added. The polymeric chlorobutadiene emulsion is then coagulated by freezing on the surface of a brine-chilled drum.

When commercial polymerization of chlorobutadiene was undertaken in an aqueous emulsion some of the employees began to lose their hair after a few weeks or months. The loss of hair could be much reduced by frequent and complete change of the air of the working environment. The hair loss was predominantly on the scalp, and hair always grew again when the employees were transferred to other occupations. Microscopical examination of the hair showed that it came out at the root, a bulb being present at one end of each hair shaft, but there was no evidence of change in the shaft itself. A composite product containing various cyclic and short-

chain polymers of chlorobutadiene was prepared ; when two drops of this was placed on the back of a mouse or guinea-pig the area covered by the solution became completely denuded of hair in 4 to 10 days. In about 3 weeks hair was again visible over the denuded area, and in 6 weeks it had completely regrown. *H. M. Vernon.*

Blood Changes in Operatives Engaged in the Preparation of Nylon. (Osservazioni sul comportamento della crasi sanguigna in alcuni operai addetti alla preparazione de nailon.) CERESA, C. (1948). *Med. d. Lavoro*, **39**, 162.

The author examined 27 nylon operatives who had been some years in the industry. Their hæmoglobin figures ranged from 68 to 90%, 9 of them having a figure under 80%. All but 4 had under 4 million red cells, and in 9 there were 3·5 million or less. All workers had a weak positive van den Bergh reaction, and serum bilirubin varied from 0·68 to 1·78 mg. per 100 ml. The nitril process in the manufacture of nylon seemed to cause the most definite van den Bergh reaction, as did also contact with adipic acid and hexamethylene diamine. Slight leucopenia occurred with the anæmia, and also a rise in the monocytes. *G. C. Pether.*

INDUSTRIAL PHYSIOLOGY

Effects of Physical Characteristics of Fabrics Upon Physiological Heat Load and Subjective Reactions. CHRISTENSEN, W. R. (1948). *J. industr. Hyg.*, **30**, 251.

The influence of the physiological heat load and physical characteristics of various cotton fabrics on the comfort of the wearers was tested in the "jungle chamber" of the Climatic Research Laboratory, Lawrence, Massachusetts. In this chamber, $60 \times 15 \times 9$ ft., the dry-bulb temperature of the air and walls was kept at 90° F., the wet-bulb at 86° F., and the wind velocity at 1·5 or 5·8 miles per hour. The test subjects were 6 to 10 soldiers. They wore U.S. Army fatigue uniforms made from 9 test fabrics, and they walked on a horizontal treadmill for an hour at 3·5 m.p.h. The physiological observations were of rectal temperature and pulse rate at the end of the exercise and of sweat secretion during it. Comments of the test subjects were restricted to the degree of coolness experienced, drag (tendency of material to adhere to skin surfaces and thereby impede motion), skin sensation in general, and overall preference. With the 1·5 m.p.h. wind the heat loads imposed by the test fabrics were found to be influenced mainly by their weight, thickness, and possibly the degree of wetting during use, but when the wind velocity was increased to 5·8 m.p.h. the heat ratings were different. Those fabrics felt to be relatively more comfortable were characterized by greater wetted area and high air permeability. Coolness, skin sensation, and drag were the most important criteria in determining the subjective acceptability of a uniform. However, subjective appraisal of heat load was found to be quite inconsistent when compared with objective results, and it appeared that the test subjects were unable to distinguish clearly between the sensation of coolness and other subjective stimuli.

H. M. Vernon.

Evidence for an Adrenergic Component in the Nervous Mechanism of Sweating in Man. HAIMOVICI, H. (1948). *Proc. Soc. exp. Biol., N.Y.*, **68**, 40.

Palmar sweating was examined by the method of Silverman and Powell (*Amer. J. med. Sci.*, 1944, **208**, 297) in 24 subjects after intravenous injection of an adrenergic-blocking agent, "dibenamine" (N,N-dibenzyl-β-chloroethylamine hydrochloride), in doses of 5 mg. per kilo of body weight. The substance decreased or abolished spontaneous palmar sweating, concomitant with a dilatation of the cutaneous vessels of the hands and fingers, as shown by skin temperature measurements. After dibenamine, intravenous injection of neosynephrine (0·5 to 1 mg.) did not stimulate sweating, while 25 mg. of mecholyl subcutaneously induced profuse sweating. It is concluded that, in addition to the known cholinergic fibres supplying the sweat glands, there is also an adrenergic component in the nervous mechanism of sweating in man. *A. Schweitzer.*

Thermal Insulation and Comfort Characteristics of Fibrous Glass-lined Garments. YAGLOU, C. P. (1948). *J. industr. Hyg.*, **30**, 312.

Fibrous glass-lined garments are alleged to offer much warmth with little weight, and to test this statement the author made some comparisons. The test garment was a fibrous-glass-lined jacket with "zipper" front. It consisted of a wind-resistant, water-repellent cotton twill shell and a light-weight inner lining, with soft laminated fibrous glass quilted between the two shells. As fibrous-glass-lined trousers could not be obtained, uncoated shearling trousers were used instead. Comparative tests were made in which garments made of wool-pile fabric were worn. Two subjects were exposed for 2½ hours to a temperature of −1° F. with air movement of 20 to 25 feet per minute. Hands and feet were protected from cold by electrically heated gloves and socks. It was found that, though the fibrous glass-lined jacket showed a higher insulation value, per pound of weight than did two wool-pile jackets, its performance on a thickness basis was poor, the mean insulation value being 37% lower. The body skin temperatures dropped faster and the subjects shivered sooner. Also the glass-lined jacket showed poor resistance to compression. Pressures which normally occurred in the back and elbows of the subjects, who sat on a wooden chair, reduced the insulation of glass lining to one-fourth the maximum value observed in parts of the jacket not subjected to compression. Under similar conditions loss of wool-pile insulation was only half as much. An advantage of fibrous glass is its relatively low adsorption of body moisture, for it was found to be less than half that of wool. *H. M. Vernon.*

The Role of Subnormal Temperature in the Aetiology of "Chills." (In Russian.) KOIRANSKI, B. B. (1948). *Gigiena*, No. 5, 18.

A review of the relevant literature is followed by an account of the author's own investigations on the effect of subnormal temperature (within a range of +10° to −10° C.) on the areas of human body unprotected by clothing and sensitive to cold ; the temperature of the skin served as an index of changes occurring in the cutaneous blood vessels as the result of chilling. The experimental (healthy) subjects (2 men and 2 women aged 20 to 30) remained for 45 minutes in a room at 21° to 23° C. ; a ribbon thermocouple was then attached to the terminal phalanx of the index finger, and skin temperature measured until it became stable ; after this a thin rubber glove was placed on the hand which was immersed for up to 120 minutes in water at 5° C. and 15° C., and the skin temperature plotted graphically. At 5° C. the minimal skin temperature was reached in 8 minutes, and afterwards fluctuated between 7° and 15° C., showing

the phenomenon of reflex hyperæmia. At 15° C., the lowest level was also reached in 8 minutes, but afterwards the skin temperature remained stable at about 15° C. during the remaining period of the immersion. Physiological evidence is adduced to show that these experimental results can be interpreted as follows. The onset of chill is due not so much to a sudden and sharp cold stimulus as to a protracted effect of subnormal temperature. *H. P. Fox.*

Estimation of the Anoxic Effect of High-altitude Flying. (Pokus o objektivní hodnocení vlivu anoxie za výškového letu.) DVOŘÁK, J., KOPECKÝ, M., and MIKULA, J. (1948). *Voj. zdravotn. Listy*, **17**, 262.

The influence of anoxia on the human organism can be estimated with considerable accuracy by the magnitude of the smallest increment or decrement of a certain intensity of light which is necessary in order to produce a sensation of a different intensity. This change, expressed as a fraction of the original intensity, is called the differential threshold.

A Pulfrich stufenphotometer (step-photometer) was used as a source of light; the beam of its lamp after passing through the appropriate colour filters and through the screen was projected on a white screen, which the subject viewed under an angle of 300 degrees. The investigation was carried out in white, red, and green light. The standard field was first adjusted by setting the drum of the photometer at 0·6 for white light, at 14·0 for red light, and at 86·0 for green light. The comparative field was obscured. The tested subject was requested to move the drum of the comparative field until its intensity equalled that of the standard field. Five to 10 comparisons were made for every colour and the magnitude of the difference of readings between the two drums was noted. The low-pressure chamber in which the investigations were carried out was subsequently obscured for 10 minutes and measurements were repeated 5 times for every colour. They were repeated once more after the pressure in the chamber had been lowered to equal the pressure at an altitude of 6,000 metres (355 mm. Hg). Measurements were carried out on 8 normal males and 4 normal females, aged 16 to 30 years. It was found that the differential threshold (the smallest difference between the readings of the two drums at which the light of the two fields was recognized by the subject as being of a different intensity) for all colours was increased by 9% at an altitude of 6,000 metres. *Jan Brod.*

An Appraisal of Intermittent Pressure Breathing as a Method of Increasing Altitude Tolerance. ECKMAN, M., BARACH, B., FOX, C., RUMSEY, C. C., SOMKIN, E., and BARACH, A. L. (1947). *J. Aviat. Med.*, **18**, 565.

Four subjects breathed 100% oxygen at ambient pressure by means of a pneumolator set to deliver gas at a mean positive pressure of 15 mm. Hg. at an altitude of 42,300 ft. The pneumolator was also used at 45,000 ft. Arterial blood samples showed that about half the mean applied pressure was transmitted to the gases of the blood. The rise in arterial oxygen saturation from 81 to 94% with the pneumolator was largely due to alkalosis resulting from hyperventilation. At ambient pressure the mean arterial CO_2 tension was 35·7 mm. Hg, with a blood *p*H of 7·46. With the pneumolator the CO_2 tension fell to 20·8 mm. Hg and the *p*H rose to 7·61. The subjects had symptoms of alkalosis, and in some cases tetany. The results suggest that the increase in arterial oxygen saturation achieved by the use of the pneumolator is offset by the effects of the hyperventilation which it induces. There is not this disadvantage when constant pressure breathing is employed.

The Hecht visual discrimination test and arithmetical problem tests were applied to 5 subjects breathing air at ambient pressure and with the pneumolator set at 0 to 28 mm. Hg at altitudes of 16,000 ft. and 17,000 ft. Observations were also made at 42,300 ft. with the pneumolator and constant pressure breathing at 15 mm. Hg. At 16,000 and 17,000 ft. there was little change in performance when the pneumolator was used. Vision was improved in one subject. In the arithmetical test the performance of 2 subjects improved, of 2 became worse, and of one was unchanged. The same average decrease in visual discrimination was found with both methods of pressure breathing at 42,300 feet. With constant pressure the arithmetical test gave the same results as at sea level. A deterioration in performance was observed when the pneumolator was used, but this was not significant. In about half the tests the subjects complained of numbness and tingling of the fingers and numbness of the lips when the pneumolator was used. There were 3 cases of overt tetany with carpopedal spasm. Two subjects preferred constant pressure breathing and 3 the pneumolator. The incidence of symptoms with the pneumolator decreased as the subjects became more experienced.

D. Mc.K. Kerslake.

Adrenal Cortex and Altitude Tolerance. KOTTKE, F. J., TAYLOR, C. B., KUBICEK, W. G., ERICKSON, D. M., and EVANS, G. T. (1948). *Amer. J. Physiol.*, **153**, 16.

In mice, resistance to low oxygen tension in decompression chambers is increased by the administration of an aqueous extract of adrenal cortex prepared by Kendall. The same effect can be demonstrated by intraperitoneal injections of glucose. Two commercial adrenal extracts and desoxycorticosterone acetate injected into the animals in large doses had no beneficial effect. In specially trained dogs, on the other hand, large doses of Kendall's extract could not ameliorate the deterioration in co-ordination, vision, and hearing in conditions of high altitude. *A. I. Suchett-Kaye.*

Effect of Hypoxia upon Temperature Regulation of Mice, Dogs, and Man. KOTTKE, F. J., PHALEN, J. S., TAYLOR, C. B., VISSCHER, M. B., and EVANS, G. T. (1948). *Amer. J. Physiol.*, **153**, 10.

This paper deals with the problem of heat regulation in animals and men subjected to hypoxia in decompression chambers. Mice, for instance, in an atmosphere of low oxygen tension became almost completely poikilothermic and muscular activity and ability to shiver were absent. Mice breathing normal air at a temperature of 20° C. died when pressure was equivalent to that at 30,000 ft., but when they were rendered hypoxic "survival ceiling" increased to 43,000 to 54,000 ft. Below 15° C. the resistance to hypoxia decreased. The protection against death at high altitude, conditioned by a drop in body temperature of mice, is due to the decreased oxygen demand at lower body temperatures. In dogs, inspiration of air with low oxygen content caused an increased loss of body heat, as compared with controls. When the oxygen content was less than 10%, shivering was regularly inhibited.

Similar experiments in men showed that during hypoxia shivering was inhibited; in addition, there was

not an increase in oxygen consumption, as seen in controls breathing normal air at gradually falling temperatures. The heat loss, as shown by skin temperatures and peripheral vascular dilatation, increased in hypoxia. These findings were noted in 4 men, but in a fifth experiment shivering was observed, and although skin temperatures rose there was no fall in rectal temperature. *A. I. Suchett-Kaye.*

INDUSTRIAL LUNG DISEASES

Cancer of the Respiratory System in the United States Chromate-producing Industry. MACHLE, W., and GREGORIUS, F. (1948). *Publ. Hlth. Rep., Wash.*, **63**, 1114.

The authors give the mortality data for the seven chromate plants in the United States, which employ 1,445 workers. They found 42 deaths from cancer of the respiratory system among a total of 193 deaths over periods varying with the different plants. Of the 193 deaths, 66 were from cancer; thus the respiratory cancers were 63·6% of all cancers, compared with 8·7% in a control group of 733 deaths among Metropolitan Life Insurance Company industrial-policy holders in the year 1946. Of these, 115 were from cancer, of which 10 were of the respiratory system. The mortality rate for lung cancers in the chromate workers at ages over 50 was up to forty times that for a comparable industrial group. In one plant exposure was restricted to bichromates and chromic acid, and here there was no cancer of the respiratory system; this evidence strongly suggested that the carcinogenic substances were the monochromates. This also means that nasal irritation and septal perforation may occur without associated high rates for cancer of the lung. The mean duration of exposure was 14·5 years.

[This is a most important paper.] *K. M. A. Perry.*

Pneumoconiosis of Coal-miners. FLETCHER, C. M. (1948). *Brit. med. J.*, **1**, 1015, 1065.

In the past 15 years more than 17,000 cases of coal-miners' pneumoconiosis have been certified in South Wales. There has been a rapid increase in certification in recent years, partly the result of the Coal-miner's Pneumoconiosis Order which made compensation payable when the disease was in the stage of reticulation, and partly the result of increased awareness of the disease coupled with opportunities of alternative employment. The increase in the disease is related to quantitative rather than qualitative differences in the dust. There is no great difference between steam-coal areas and anthracite areas; while the incidence is higher in South Wales than in the rest of the United Kingdom the dust concentration is greater in South Wales than elsewhere. High concentration is due in the anthracite mines mainly to poor ventilation, which was especially bad during the nineteen-twenties, and in the steam-coal mines to the introduction of intensive mechanical methods of mining in the dusty coal-seams of East Glamorgan during the next decade.

Areas of severe emphysema known as "focal emphysema" around the coal foci in the lungs are the main cause of the shortness of breath from which the miners suffer. Superimposed on this focal disease is a progressive massive fibrosis, which may continue to progress after the worker leaves the mines. Its development appears to be independent of continued dust exposure. So long as the disease is confined to coal nodulation and the associated focal emphysema it generally ceases to progress if the man stops working in a high concentration of dust. Massive fibrosis associated with a raised erythrocyte sedimentation rate is progressive; it suggests infection, perhaps tuberculous, superimposed upon a lung already occupied by dust. Nevertheless, tuberculosis may often be recognized as a separate disease in addition to pneumoconiosis. Therapy is only symptomatic but much may be done by reassurance, breathing exercises, and the use of antispasmodics in certain more advanced cases. Post-mining employment in certified cases is important. Special provisions are needed in addition to those already planned. *K. M. A. Perry.*

The Blood Picture in Miners' Pneumoconiosis. (Het bloedbeeld bij mijnwerlers-pneumoconiose.) CREYGHTON, J. (1948). *Geneesk. Gids*, **26**, 179.

A comparative study of the blood picture in 59 cases of pneumoconiosis at the respective stages of reticulation (21), nodulation (16), and consolidation (22) shows that a deviation from the normal—moderate increase of the erythrocyte sedimentation rate (E.S.R.)—occurred only in one-third of cases at the consolidation stage. Where tuberculosis was associated (38 cases) the E.S.R. was high in two-thirds of cases and a shift to the left in the differential white cell count was observed in one-third.

A. Lilker.

Some Aspects of the Evolution of Silicotic Lesions. COSTERO, I. (1948). *Amer. J. Path.*, **24**, 49.

The author studied 35 cases of pulmonary silicosis. The structure and evolution of the silicotic nodes are discussed in the light of his investigations with the silver impregnation stains and stains for elastic tissue. The technical methods of Rio-Hortega and Gallego are described and there are many illustrations. The author concludes that the histological basis of all silicotic lesions of the human lung is the proliferation of the reticular fibres, that the nodules grow by apposition of adjacent nodes, and by incorporation of surrounding lung tissue damaged by collapse or "desquamative pneumonia." The elastic fibres disappear in the complete lesions. The diffuse silicotic lesions, which he describes as fibrous plaques, peribronchial sclerosis, and pleuritis, have a histogenesis, structure, and evolution similar to those of the typical silicotic nodule.

Douglas H. Collins.

Apparatus for Dispensing Aluminium Dust in the Treatment of Silicotics. CHURCH, F. W., and INGRAM, F. R. (1948). *J. industr. Hyg.*, **30**, 246.

In the employment of aluminium hydroxide for treatment of advanced silicosis, no control has been exercised on the amount of dust inhaled by the patients, but the dosage has depended on the anatomical position and inspiratory effort of the patient. In order to provide a dust dispenser by which the dosage could be accurately maintained, the apparatus used by Schrenk was modified and improved, so that all subjects were continuously exposed to the same predetermined concentration of dust. The aluminium hydroxide used was ground to an average particle size of 2 μ. An air-tight box, 4×4×4 ft. (1·2×1·2×1·2 m.) was constructed, and at one end was fixed a plenum chamber 10 in. wide and extending the full width and height of the box. Dust-laden air entered the box at the top through a 6-inch pipe, and was distributed uniformly in the box at a low

velocity. It was withdrawn into the plenum chamber through a 3 in. × 4 ft. opening at the bottom, and thence into a filter unit discharging outside the building. Of the 9 openings at the sides of the box, 6 served as take-off points for administering the dust to patients, and 3, leading to fresh air, served as controls. Each take-off point had a two-way diaphragm valve through which a patient could inhale the dust, and then exhale it into a waste pipe. By a complicated device, described in detail in the paper, dust was introduced into the box at a constant rate, usually 300 million particles per cubic foot of air. Numerical data are recorded showing the average particle size of the dust and its distribution in the box. *H. M. Vernon.*

Further Observations of Lung Changes Associated with the Manufacture of Alumina Abrasives. SHAVER, C. G. (1948). *Radiology*. **50**, 760.

Twelve months after his first report (*J. industr. Hyg.*, 1947, **29**, 145) the author has found 34 employees engaged in the manufacture of alumina abrasives with well-established radiological abnormalities and 38 early cases. Symptoms and physical signs are shown only by those with well-established radiological changes. In 1 man the radiograph was normal when he left the industry; 15 months later it showed granular shadows in the upper part of each lung. Although present experience suggests that once the disease is well established progression is usually rapid, there is evidence that removal of men from exposure when the earliest radiological changes are found will commonly prevent the development of serious disability. Seven case histories are given. The author states that although the fume contained 35% of silica, mainly of very fine particle size, he does not think that the changes in the lungs were due to this substance. *H. E. Harding.*

The Fume Exposure in the Manufacture of Alumina Abrasives from Bauxite. JEPHCOTT, C. M., JOHNSTON, J. H., and FINLAY, G. R. (1948). *J. industr. Hyg.*, **30**, 145.

The lungs of workmen exposed to the fumes given off by the electric furnaces used in the manufacture of alumina abrasive from bauxite have been found to contain alumina. This paper describes the results obtained in four Canadian plants manufacturing the abrasive. Air samples were analysed by several different methods. The results varied and in any case particles of less than 0·25 μ were not included; electron-microscope observations showed that many particles were much smaller than this. Dust counts made by an impinger method revealed that air samples taken near the furnaces contained 11,000,000 to 300,000,000 particles per cubic foot. The mean weight of dust per cubic metre of air ranged from 12 to 106 mg. The samples contained 17 to 42% of silica and 45 to 62% of alumina. Samples of fume collected 1 to 10 feet above the furnaces by a vacuum cleaner containing the usual cotton bag contained 29 to 44% of SiO_2 and 41 to 62% of Al_2O_3. Lung tissue was obtained at necropsy on 4 workmen who had been exposed to fumes for 3 to 5 years. The total dried ash of the tissue amounted to about 6%, or nearly the same as in normal persons, but from 0·9 to 2·4% of it was in the form of silica, as contrasted with 0·07% in normal lungs; also 1·2 to 2·4% was in the form of alumina. Analyses of urine for alumina did not show much difference from the controls. *H. M. Vernon.*

The Effect of the Use of Calcined Alumina in China Biscuit Placing on the Health of the Workmen. A Field Study in a Group of Pottery Workers in North Staffordshire. MEIKLEJOHN, A., and JONES, W. W. (1948). *J. industr. Hyg.*, **30**, 160.

Until 1925 fine-powdered flint was used for "placing" china ware for the purpose of biscuit firing. Since then calcined alumina (corundum) has been gradually substituted for the flint, and its use is now established throughout the industry in England. Potters' rot or potters' asthma was very common among china biscuit placers, and under the British silicosis scheme men using flint were (after 1931) required to be medically examined every 18 months. When alumina was substituted the examinations were discontinued. In the present inquiry 52 china-biscuit placers who had previously been examined by the Silicosis Medical Board were re-examined. All had been exposed for a considerable time to flint, followed by exposure to alumina for 2 to 16 years. The workmen were convinced that alumina produced a dustier atmosphere than flint, but it did not, like flint, irritate the nose and throat, or induce a feeling of stuffiness on the chest, and the men no longer feared the effects of the dust. They appeared much healthier than the old-time flint placers, though complaints of cough, expectoration, and dyspnœa were as frequent as before. An *x*-ray examination indicated that in 6 of the men there was progression of the disease, this being no better than would have been expected if the men had continued to work with flint. However, no evidence was obtained that the alumina was responsible for the adverse effect, and this conclusion was supported by the opinion of the Medical Board. In 1937 they examined 50 men employed in the manufacture of aluminium from alumina and concluded that "there is no evidence of pneumoconiosis or of any other pulmonary disease arising from the considerable dust risk (alumina) to which these men have been exposed." In 1946, 44 of these workmen were alive and well and still at their jobs; the remaining 6 had died from causes unrelated to pulmonary disease. *H. M. Vernon.*

***Aerobacter cloacæ* Endotoxin as a Possible Factor in the Etiology of Bagassosis.** SCHNEITER, R., REINHART, W. H., and CAMINITA, B. H. (1948). *J. industr. Hyg.*, **30**, 238.

The present investigation was made in order to ascertain whether *A. cloacæ* and its toxin were present in bagasse. Thirty-eight samples of bagasse were examined by the serial dilution method. Plate counts of micro-organisms from raw bagasse ranged from 100 to 305,000,000 per g.; those from processed bagasse from 1,700 to 170,000 per g.; from plant dust and sawdust from 90,000 to 38,000,000 per g.; and from factory air samples from 40 to 5,280 per c. ft. Thirty-eight cultures resembling *A. cloacæ* were selected from 11 samples, purified, and studied by biochemical and serological methods, and 23 were identified as *A. cloacæ*. The endotoxin liberated by *A. cloacæ* was demonstrated in sterile saline extracts from three samples of bagasse contaminated with this organism and from one sample in which its presence could not be confirmed. Although this evidence suggests *A. cloacæ* as a factor in the ætiology of bagassosis, it must be stressed that bagassosis is not identical with the acute respiratory disease caused by *A. cloacæ* in cotton workers. The differences observed may be due partly to variation in the quantity and potency of the toxin contained in the dust, and in the amount of dust inhaled. Again, bagasse dust can

penetrate into lung tissue where it becomes embedded, but cotton dust, though it reaches the alveoli of the lungs, has never been found embedded in the tissue. It would seem, therefore, that the greater severity and duration of symptoms in bagasse workers than in cotton workers may be due to the combined action of *A. cloacæ* and an irritant dust. *H. M. Vernon.*

Delayed Chemical Pneumonitis or Diffuse Granulomatosis of the Lung Due to Beryllium. WILSON, S. A. (1948). *Radiology*, **50**, 770.

Changes in the lungs have been found in workers engaged in extracting beryllium from its ore, in the manufacture of beryllium salts and oxides, in the production of beryllium alloys, in the preparation of the phosphors used in coating fluorescent lamps and neon tubes, and in the manufacture of such lamps and tubes.

The disease appears in two forms, an acute pneumonitis and a chronic diffuse granulomatosis of the lungs, but there is some overlapping between the two groups. Radiologically in the acute type there is a diffuse haziness or ground-glass appearance similar to that of pulmonary œdema but not usually visible until 1 to 3 weeks after the onset of symptoms. This appearance is succeeded by one of soft shadows resembling those of bronchopneumonia, accompanied by prominent linear markings and enlargement of the hilar shadow. All these shadows usually disappear completely within a few months. The chronic form has a latent period that may extend to more than 3 years after exposure. The radiographic appearances are described in 3 stages. The first stage is marked by a fine diffuse granularity, presenting a fine sandpaper appearance, which under the magnification of a reading glass suggests a sandstorm: the lesion is uniform, diffuse, and particulate, and the picture is said to be unlike that of any other lung condition. In the second stage a diffuse reticular pattern is added to the granular background, while distinct nodules of 1 to 5 mm. diameter appear in the third stage. Many, but not all, cases progress through all three stages, but the amount of physical disability does not correspond at all closely with the degree of involvement of the lungs shown in the radiographs. *H. E. Harding.*

On the Retention of Air-borne Particulates in the Human Lung. LANDAHL, H. D., and HERRMANN, R. G. (1948). *J. industr. Hyg.*, **30**, 181.

The degree of retention of air-borne particles in the lung depends on the diameter of the particles, the rate of flow of air in the respiratory passages, the tidal air, the rate of respiration, and on certain physical properties of the particles.

In the various tests corn oil was chosen to represent a non-hygroscopic liquid of about unit density (0·914). The air breathed contained about 1 mg. per litre of the oil. Other tests were carried out with sodium bicarbonate dust and with atomized solutions of the bicarbonate; also with a cloud of tricalcium phosphate, with methylene blue atomized as an aqueous solution, and with a 5% solution of the very hygroscopic glycerol. The larger the particles the greater the retention. For very small particles the retention is negligible except for the process of diffusion (Brownian movement), which becomes more effective the smaller the particle. Thus at a certain particle size retention is at a minimum. When the tidal air is increased or the frequency of respiration is decreased at a constant inspiratory flow rate the retention greatly increases because of greater settling and diffusion. The effect of changing the inspiratory flow rate for a constant breathing pattern was shown by the fact that the particle diameter for 50% retention of $NaHCO_3$ at 18 litres per minute was 0·8 μ, while at 60 litres per minute it was only 0·3 μ.

The following values were found for the particle diameters corresponding to a 50% retention when the respiration rate was 15 per minute and the tidal air 450 ml.: corn oil, 3 μ; $Ca_3(PO_4)_2$, 1·5; methylene blue, 1·2; $NaHCO_3$ dust, 0·9; and glycerol, 0·7.
H. M. Vernon.

Electron-microscopical Studies of Industrial Dust. (Über die Untersuchung von gewerblichen Stauben im Elektronenmikroskop.) JOHN, M. (1948). *Wien. med Wschr.*, **98**, 318.

The author points out that with the electron microscope dusts may be examined in a manner previously impossible. Early work in this field was described by Friese and Müller in 1939, and the present author continued these investigations, though on a smaller scale than was first intended. He examined dusts obtained by boring or other methods from various mines, quarries, and factories. These had a basis of quartz, asbestos, copper ore, siliceous rock, sericite, and other minerals. The microscope revealed that many small particles, hitherto considered round and relatively innocuous, were in fact sharp and doubtless pathogenic. Moreover, it appeared that wet boring gave a much smaller degree of protection to the operative than was hitherto believed. Photographs from a much larger series are given, all being taken to indicate an enlargement of 1 : 37,000, so that 37 mm. of the photograph corresponded to 1 μ or 0·001 mm. of the original. In the dusts collected during wet boring, particles of the order of 0·1 to 0·002 μ were found at a considerable distance from the working site. The author thinks that the mere presence of silicon dioxide in inhaled dust does not of itself indicate a definite hazard. *G. C. Pether.*

INDUSTRIAL DERMATITIS

Clinical, Histological, and Biological Study of Skin Reactions Provoked by Chinese Lacquer. (Etude clinique, histologique et biologique des réactions cutanées provoquées par la laque indochinoise.) PELLERAT, J., CHMEL, L., and CHAMARD, R. (1948). *Arch. Mal. prof.*, **9**, 269.

Patch tests of Chinese lacquer undiluted and in varying dilutions were performed on: (1) subjects with normal skin; (2) subjects suffering from chronic eczema; and (3) subjects with various skin diseases produced reactions varying from erythematous to bullous in severity. Subjects in group (2) suffered the most severe and prolonged reactions and in some there was an exacerbation of a quiescent dermatitis. Biopsy examination on subjects with normal skin showed that the essential lesion was vesiculation. Patch tests and biopsies performed on guinea-pigs and rats gave similar results.

The appearance of lesions after the application of Chinese lacquer is highly suggestive that histamine is the intermediate causal agent. Application of lacquer to papules raised by the intracutaneous injection of a watery solution of dimethylaminopropyldibenzothiazine ("3277 R.P.," an antihistamine substance derived from phenothiazine) does not produce skin reactions. The similar injection of serum is not protective. Subcutaneous injection of dimethylaminopropyldibenzothiazine protects for 1 hour against the application of lacquer to the skin. No reaction follows when lacquer

is applied within 1 hour of painting the skin with dimethylaminopropyldibenzothiazine. The application of paraffin oil gives lesser, but not negligible, protection. The authors claim that these results are significant in providing further proof of the role of histamine in producing skin reaction following the application of vesicants, and in suggesting means of prophylaxis against vesicants. *T. A. Lloyd Davies.*

Spinner's Cancer of Lower Lip. (Spinnerinnenkrebs der Unterlippe.) KORBLER, J. (1948). *Krebsarzt*, **3**, 201.

At the Radium Institute at Zagreb, of 609 patients treated for cancer of the lower lip, 57 were women—a high rate for females. None of them smoked. The author wonders if the habit of the Croatian women of moistening with their lips the wool, linen, or hemp while spinning may not be responsible. He briefly describes 7 squamous-cell cancers and 1 precancerous state of the lip in spinners.

Skin Lesions in Persons Exposed to Beryllium Compounds. GRIEF, R. S., NASH, P., and FRIEMAN, D. G. (1948). *J. industr. Hyg.*, **30**, 228.

The skin lesions hitherto noted as being associated with the industrial use of beryllium are: (1) contact dermatitis, (2) skin ulcer, and (3) pulmonary granulomatosis arising spontaneously in patients with the chronic type of lung disease. The authors now describe subcutaneous granuloma occurring in persons who cut themselves on fluorescent lamps. Three instances of such cuts are here described, and in all of them subcutaneous granulomata developed, the histology of which is very like that of sarcoidosis of the skin. The compound with which the inside of the lamps was coated was zinc manganese beryllium silicate.

In case (1) a 12-year-old boy was playing with an old lamp; pieces of the glass entered his neck and, though the small wounds quickly healed, lumps appeared later on, and 3 months after the accident had formed a firm tumour (2·0×2·5 cm.), attached to the subcutaneous tissues. It contained a small piece of glass, and the tissue was found to contain 27 μg. of beryllium per 100 g. Microscopical examination showed numerous tuberculoid granulomata embedded in fibrous stroma. They consisted of typical epithelioid cells, and many giant cells both of Langhans and of foreign-body type were present, some of them containing concentrically laminated inclusion bodies. In case (2) a man cut a finger on a fluorescent lamp. The cut did not heal properly, and so the entire area of the wound was excised. Microscopical examination revealed the presence of numerous tuberculoid granulomata, and scattered giant cells were present. In case (3) a man who worked at a lamp factory sustained a finger-puncture from a broken lamp. Subsequently a nodule developed, which was excised. Microscopical examination disclosed a picture similar to that seen in the two previous cases. The granulomata described are similar to the skin lesions of two beryllium workers with pulmonary granulomatosis, and essentially similar to the lung lesions in this disease. *H. M. Vernon.*

ACCIDENTS AND ORTHOPÆDIC SURGERY

Late Reactions to Metallic Foreign Bodies. BOTSFORD, T. W., and FRENI, D. R. (1948). *New Engl. J. Med.*, **238**, 385.

The problem of late reactions to metallic foreign bodies has assumed a new importance as a result of war injuries. After a time such foreign bodies become encapsulated in fibrous tissues and the majority cause no symptoms. Some, however, eventually give rise to trouble, and it is then necessary to consider the problem in the light of the case history and the new symptoms, and ascertain whether the foreign body itself is the cause of trouble or whether there is some infection arising around it, perhaps blood-borne from some distal site of chronic infection, which may itself require irradication. Generally speaking, the cases fall into three groups: (1) Multiple small regional foreign bodies with cellulitis; removal of these metallic particles is usually out of the question and the problem is one of infection of soft tissue and scar. (2) Single or multiple foreign bodies with abscess formation; here the removal of the metallic fragments is often important. (3) Single foreign bodies causing local pain; removal of these is generally essential. Usually the fibrous capsule should be removed with the foreign body.

The authors give penicillin to all patients with signs of infection. In cases in which there is no infection and removal of the foreign body is contemplated, penicillin therapy is started the day before operation and continued until the wound is healed. A booster dose of tetanus toxoid is also given. Accurate location of the foreign body before operation is essential, and various modifications of *x*-ray technique may be employed for this, the Berman electro-magnetic locator, introduced by Moorhead, can be of help during the actual operation.
R. Weedon Butler.

ENVIRONMENT

Measurement of Alpha-active Dust in the Atmosphere. CARMICHAEL, H., and TUNNICLIFFE, P. R. (1948). *J. industr. Hyg.*, **30**, 211.

The authors of this paper are scientific officers of the United Kingdom Ministry of Supply, who are at present working with the National Research Council, Atomic Energy Project, Ontario, Canada. They point out that the absorption into the body, by breathing, of long-lived α-active elements such as uranium, plutonium, and radium constitutes a very serious hazard to health in operations involving these substances. It is therefore imperative to have a reliable routine method for measuring the quantity of long-lived α-active matter present in the air at any time. The permissible concentration of this matter is extremely small (for plutonium it is only 70 disintegrations per cu. metre of air per minute). At the same time the air may contain a large amount of short-lived α-particle activity of natural origin (the radon normally present in the atmosphere may give rise to 3,000 disintegrations per cu. metre per minute). Hence it is necessary to concentrate the active matter from several cubic metres of air by electrostatic precipitation or by suction through a suitable paper filter, and allow the α-particle activity arising from the radon and thoron present to decay for about 6 hours, before the plutonium activity can be measured. At the beginning of the century it was found that air confined in mines or cellars had a much greater conductivity, as measured by an electroscope, than ordinary atmospheric air. This was due to the diffusion of radon and thoron out of the ground. These gaseous radioactive elements arise from the uranium and thorium which pervade all surface minerals in concentrations of a few parts per million, and their decay products attach themselves to the dust particles in the atmosphere.

The filter apparatus employed consists of a perforated steel tube, 6 in. (15 cm.) long and 1½ in. (3·75 cm.) in

diameter. A single layer of filter paper is wrapped round, with edges overlapping, and air is drawn through the filter by means of a tank-type household vacuum cleaner, the dust being deposited on the portions of the filter paper exposed by the perforations. The precipitator has a central electrode carrying a corona disc with 50 sharp saw-teeth and a stainless-steel collecting-tube coaxial with the central electrode. A negative potential of 9,000 volts produces a brush discharge from the disc. The removable inserts of both filter and precipitator can be put into a special counter of the methane proportional type. This counter detects only the α contamination of the dust even in the presence of strong β-particle activity. After insertion of a sample in the counter the air must be displaced by methane before counting begins.

Numerous measurements were made with different rates of air flow and different voltages, and the losses of dust were determined. The suction rate of air provided by the vacuum cleaner was 2·0 cu. metres per minute in the electrostatic apparatus, and 0·8 cu. metre in the filter apparatus. Extraction of dust at these rates of flow was 40% for the precipitator and 100% for the filter. Counting efficiency was 49% for the precipitator but only 14% for the filter, owing to penetration of the dust into the paper. The overall counting yield of the precipitator was nearly 4 times that of the filter, and in practice it is desirable to employ both types of apparatus.

H. M. Vernon.

Employment of a Nephelometer for Determination of the Concentration and Size of Smoke Particles in the Air of Industrial Premises. (In Russian.) SHAGAN, I. B. (1948). *Gigiena*, No. 7, 20.

The apparatus (a nephelometer of Russian make) is described and illustrated and its use is explained. To facilitate work on industrial premises, a portable accessory model, consisting of 6 parts carried in a case the size of that for portable microscopes, was designed and constructed. With this set in any part of the industrial premises in 3 to 5 minutes the concentration and average size of smoke particles can be determined from previously calculated graduated graphs. A selected case (determination of zinc-oxide smoke particles) is presented in which the size of particles was calculated by the Stokes formula with Cunningham's correction. Nephelometric determinations were fairly accurate, agreeing within very narrow limits with the actual measurements of smoke particles by the electron microscope.

H. P. Fox.

Conditions of Work and Hygienic Measures in the Mining of Ozocerite. (In Russian.) BRAGINSKI, P. L. (1948). *Gigiena*, No. 5, 24.

The paper is a précis of the work of a special team of the Kiev Institute of Hygiene of Labour and Vocational Diseases. The chief danger in the mines is the presence of gases consisting of heavy and light saturated and unsaturated aliphatic, as well as aromatic hydrocarbons, which are adsorbed on the ozocerite and the rock in which the mineral is embedded. The air in the mines also contains carbon dioxide, hydrogen sulphide, and sulphur dioxide, which probably seep through from nearby oil wells. Clinical observations showed that the gases present in the ozocerite mines have a selective effect on the hypothalamus, sometimes causing delirium. Some hygienic measures directed towards improvement of ventilation and reduction of gas concentration in the mines have been taken, with favourable results.

H. P. Fox.

GENERAL

Phosphorus in Hygiene Assessments of Water. (In Russian.) OBUKHOV, P. F. (1948). *Gigiena*, No. 5, 15.

Regular tests were made with water from the river Kama, in the vicinity of the city of Molotov, and from five smaller streams (of which 3 were under observation for more than 2 hydrological years) to determine organic phosphorus and suspended and dissolved phosphates during the various months of the year; water samples were obtained above the city, within it, and at about 0·5 kilometre below the mouth of the main sewer. The total phosphorus (in mg. per litre) varied at these 3 sites from 0·450 to 2·595, from 0·210 to 0·255, from 0·175 to 0·762, and from 0·083 to 1·230 during February, May, August, and December respectively, the corresponding water flow being 698, 4,068, 570, and 997 cm. per second. The increase in total phosphorus was apparent in samples obtained within or below the city, and was correlated with the worsening of the accepted indices of water pollution. Water samples obtained from springs and artesian and dug wells showed a total phosphorus content not exceeding 0·2 mg. per litre in all "natural" waters, this figure being accepted as a hygienic normal standard for the Molotov Province. It was found that the presence of dissolved phosphates over 0·05 to 0·07 mg. per litre indicates a recent pollution of the water.

H. P. Fox.

Use of Mixed Coagulants for Purification of Drinking Water. (In Russian.) KULSKII, L. A., and KOGANOVSKI, A. M. (1948). *Gigiena*, No. 6, 6.

The process of coagulation was studied in drinking water containing humin (humic acid?) by the use of aluminium sulphate and ferric chloride coagulants in the following ratios (in g. per 100 g.): 75, 50, 40, and 25 of $Al_2(SO_4)_3$ to 25, 50, 60, and 75 of $FeCl_3$; the pure coagulants served as controls. Tabulated results show that coagulation was markedly accelerated and intensified when the aluminium-sulphate to iron-chloride ratio was within the range from 50 : 50 to 25 : 75; sedimentation of the precipitate was also considerably accelerated. Further tests were concerned with the rates of coagulation and sedimentation as correlated with the composition of the mixed coagulants in the absence and presence of humic acid and as conditioned by the *p*H of drinking water. The results indicated the feasibility of using mixed coagulants for the purification of drinking water.

H. P. Fox.

Chlorination of Well Water. (In Russian.) GABOVITCH, R. D. (1948). *Gigiena*, No. 6, 10.

Bacteriological analyses of natural well water, and of that from wells artificially infected with *Bacterium coli*, *Salmonella* spp., paratyphoid organisms, and a mixture of dysentery organisms showed that the ordinary chlorination procedure was unsafe when the residual chlorine fell below 0·5 to 0·6 mg. per litre. In those cases in which chlorination requirements of well water could be determined, a dose of 1·5 to 6 mg. of chlorine per litre of water was found safe; where chlorination requirements were unknown, superchlorination (15 to 20 mg. of chlorine per litre of water), followed by the addition of 400 mg. of hyposulphite (aqueous solution or tablets) per bucket, was effective. *H. P. Fox.*

Purification of Water by Electrolysis with Iron Electrodes. (In Russian.) IZYUROVA, A. I., and OVCHINKIN, I. P. (1948). *Gigiena*, No. 7, 5.

Although purification of water by electrolysis with iron instead of aluminium electrodes is efficient, fairly large amounts of ferrous and ferric compounds are formed in the process—up to 21·3 mg. per litre in 60 minutes. For this reason, a subsequent filtration (after electrolysis) through a sand filter accelerates clarification of water which otherwise is very turbid owing to the slow coagulation of ferrous compounds. With main drainage water, containing small amounts of dissolved oxygen, additional oxidation may be attained by aeration or by the introduction of supplementary insoluble anodes of graphite or nickel. The bacterial count in water purified with the aid of iron electrodes is low, but if this water is to be used for drinking further disinfection by chlorination or additional electrolysis is recommended. Drinking water of standard quality was obtained from dirty pond water after 15 minutes' electrolysis with iron electrodes, subsequent filtration, and supplementary electrolysis for 15 minutes with the aid of carbon electrodes. Electric power consumption, under laboratory conditions, was high, but it is thought that this item can be reduced in large-scale installations. Tabulated data show the effect of electrolysis on the physico-chemical composition of water; aeration of water; rate of oxidation of ferrrous compounds; purification of main drainage water with subsequent filtration; and disinfection of dirty pond water by supplementary electrolysis. *H. P. Fox.*

Bactericidal Properties of Chloramines and Free Chlorine in Water. BUTTERFIELD, C. T. (1948). *Publ. Hlth Rep., Wash.*, **63**, 934.

For the disinfection of water it is known that sufficient chlorine must be added to satisfy the chlorine demand of the water and provide a residual chlorine concentration which will increase disinfection. Unfortunately the bactericidal results with standard amounts of residual chlorine have been inconsistent and often unsatisfactory. It is now known that free chlorine is a better disinfecting agent than chloramines, that the standard *ortho*-tolidine test does not differentiate between free chlorine and chloramine residuals, that *p*H and temperature affect the efficiency of free chlorine and chloramine, and that failure to differentiate between free chlorine and chloramine has led to inconstant and unsatisfactory results. Studies were made of the bactericidal properties of both these agents separately at different *p*H values and at different temperatures, a number of differing organisms being used.

From figures reproduced it is seen that, exactly at break point, no free chlorine or chloramine remains; it can be shown that at this point no bactericidal action occurs. From a study of these figures it is also quite evident that free chlorine is a much better bactericidal agent than chloramine. It is also thought that the proper use of free chlorine will eliminate many undesirable tastes and odours.

The position may be summarized thus: (1) The longer the time of contact between organisms and disinfecting medium the more effective the sterilization. (2) The higher the temperature of the water in which the contact is made, the better the sterilization. (3) The higher the *p*H of the water in which the contact is made, the poorer the sterilization. (4) Other things being equal, it takes very much longer to sterilize water with chloramine than with free chlorine, unless the amount of chloramine is 25 times that of free chlorine needed. (5) When similar amounts of residual chloramine and free chlorine are used the contact period for chloramine must be 100 times that for chlorine if a 100% kill is to be obtained. *Cecil Herington.*

Technique of Determination of *Bacterium coli* in Soil. (In Russian.) GODLEVSKAYA, M. V. (1948). *Gigiena*, No. 6, 16.

Soil samples obtained in the city of Saratov and its environs were sown direct on various liquid and solid culture media, or, in the form of soil sediment (recovered from membrane filters after filtration of soil suspension), were seeded direct on the same culture media. The technique of seeding is described in detail. The best results were recorded with a liquid medium, and carbolized Endo solid medium. Most of the *Bacterium coli* recovered from the soil belonged to the *ærogenes* and *citrovorum* strains, capable of producing fermentation on Bouril's medium at 43° C. Direct seeding of the soil on the solid culture media was preferable to sowing in liquid media; it curtailed the period of analysis by 24 hours, was economical of material and glassware, excluded antagonistic action of other organisms on *Bact. coli*, ensured a complete differentiation of all *coli* strains, and made possible their precise quantitative determination. *H. P. Fox.*

Survival of Bacteria in a Precooked, Fresh-frozen Food. GUNDERSON, M. F., and ROSE, K. D. (1948). *Food Res.*, **13**, 254.

Chicken chow min (a cooked chicken food consisting of chicken meat, noodles, vegetables, and sauce, with a *p*H of 6 and containing much colloid matter—mainly fat) was contaminated with strains of *Bacterium coli*, *Salmonella*, and *Bact. ærogenes*, 0·5 ml. quantities of 16-hour to 20-hour broth cultures being inoculated into 250 g. quantities of the sterile food. Sampling was performed by shaking 1 in 10 dilutions of samples of the food in sterile wide-mouthed bottles and carrying out further dilutions and platings from these. Counts were made on appropriate media. Primary counts were made and the material stored at −14° F. The change in bacterial count during the storage period of 9 months was studied; there was a rapid decline until the fourteenth day, after which a more or less stable population remained.

No particular effect appeared to be produced by the colloid content of the food, though previous work on cherry juice and strawberries indicated that physical consistency of the suspension media may have a bearing on survival. Among organisms tested in these investigations 20% of *Salmonella typhimurium* and 8% of *Salm. paratyphi B* survived for 9 months. Survival of the normal flora in boned chicken and chicken chow min at the same temperature was also investigated. Samples diluted 1 in 10 were mixed in a Waring blendor. Cultures showed a sharp reduction in coliform bacteria with slow decrease in total organisms. Since even the organisms for which they are used are inhibited by selective media to a certain degree, counts of both *Bact. coli* and *Bact. ærogenes* were lower on violet red bile agar than on tryptone glucose extract agar. Furthermore, the ratio of viable counts on these two media steadily fell as samples from −14° F. were examined at intervals.

Thus, cold storage renders viable organisms more susceptible to inhibitory substances, and selective media may give only 12 to 25% accurate results in the bacteriological examination of cold-stored food. Cold-stored

chicken salad was also examined; 5 out of 8 samples contained hæmolytic *Staphylococcus aureus*.

G. T. L. Archer.

Survival of *Salmonella* in Reconstituted Egg Powder Subjected to Holding and Scrambling. SOLOWEY, M., and CALESNICK, E. J. (1948). *Food Res.*, **13**, 216.

Batches of reconstituted egg contaminated with 800 to 8,000 *Salm. oranienburg*, *Salm. pullorum*, or *Salm. senftenberg* per g. were scrambled both before, and at 2, 4, 6, and 24 hour intervals after, holding at room temperature. Salmonella strains were recovered from 84 to 287 specimens; 9 out of 28 specimens held at 5° C. were also positive. Positive results were obtained from eggs scrambled immediately after reconstitution but more frequently after prolonged holding at room temperature. Cooking times varied from less than 1 minute to 7 minutes and approximately one third of samples were positive after cooking by either the beaker or the skillet method, including 2 after cooking for 7 to 8 minutes at a temperature of 69° to 72° C. Similar results were obtained with larger quantities and prolonged cooking time. Naturally contaminated egg was also scrambled, with approximately 25% positive results from specimens held at room temperature. In this case no positive results were obtained from samples held at 5° C.

"It is evident that the common methods of scrambling egg cannot be depended upon to destroy (salmonella) organisms in contaminated egg"; rapid multiplication in reconstituted egg indicates the desirability for its immediate use after reconstitution.

G. T. L. Archer.

Results of Vaccination Against Influenza during the Epidemic of 1947. LOOSLI, C. G., SCHOENBERGER, J., and BARNETT, G. (1948). *J. Lab. clin. Med.*, **33**, 789.

Between November and December, 1946, influenza vaccine trials were carried out on Chicago University students living in communities: 790 students were vaccinated, and 1,230 living in comparable conditions were observed as controls. The vaccine was composed of 25% PR8, 25% Weiss, and 50% Lee virus. The response to vaccination was satisfactory, as shown by the serum-antibody titres attained. An epidemic of influenza occurred in February and March, 1947. The attack rate was the same in vaccinated and control groups (9·5%); 2·5% of vaccinated subjects and 2·26% of controls were admitted to hospital. Acute and convalescent sera were collected from 192 unvaccinated patients with influenza; no rise of Lee antibodies was seen, but 40% of serum pairs showed a fourfold or greater rise in PR8 antibodies.

From a series of 32 throat washings 2 strains of virus were isolated by allantoic inoculation in the presence of penicillin and streptomycin. There was no close antigenic relationship between these strains and the A strains used in the vaccine, though they were evidently A in type, the failure of the vaccine to protect was not due to the long time interval between vaccination and the beginning of the epidemic, but to the lack of sufficient antigenic identity with the prevalent strains. *D. J. Bauer.*

Results of Influenza Vaccination in Industry During the 1947 Epidemic. BAETJER, A. M. (1948). *Industr. Med.*, **17**, 171.

An influenza A and B vaccine was given in certain factories during the winter of 1946–7. The expected epidemic in 1947 yielded a low incidence of cases, and these were mild. The responsible virus was influenza A, but the strains were antigenically different from those in the vaccine. Thirteen industrial companies scattered throughout the United States were able to supply records for the comparison of vaccinated and non-vaccinated groups. A warning is given of the difficulty of verifying a diagnosis of influenza, and of the bias caused by the fact that those who know that they are susceptible more readily accept voluntary vaccination. It is also difficult to choose groups similar in age and sex distribution. In these 13 companies about 37,000 people were vaccinated and 40,000 not. In 7 of them there was no real difference between the incidence of influenza in the vaccinated and in the controls. A lower rate in the vaccinated group was reported by 6 companies, but for various reasons this was not thought to be due to the vaccine. Immediate reactions to the vaccine were reported, but the percentage of employees who lost time was small. The author suggests that the results are inconclusive because the sickness records provided were inadequate, the epidemic was mild, and there were antigenic differences between the epidemic virus and the viruses of the vaccine. Similar results to these had been reported from a university group and from establishments of the U.S. Army. They do not necessarily mean that influenza vaccination will be of no value in future epidemics. *J. N. Agate.*

Toxicological Investigations of Compounds Proposed for Use as Insect Repellents. (A) Local and Systemic Effects following Topical Skin Application. (B) Acute Oral Toxicity. (C) Pathological Examination. DRAIZE, J. H., ALVAREZ, E., WHITESELL, M. F., WOODARD, G., HAGAN, E. C., and NELSON, A. A. (1948). *J. Pharmacol.*, **93**, 26.

During the war toxicological tests were conducted on some 4,000 compounds prepared by universities and chemical concerns and submitted by them for use as repellents. Only 18 of these repellents passed the final rigorous tests and were deemed safe for use by military personnel. The reader is referred to the original for the names of the preparations and the details concerning their effects on the animals tested.

PROCEEDINGS OF THE ASSOCIATION OF INDUSTRIAL MEDICAL OFFICERS

FIFTY-THIRD MEETING

The Fifty-Third (Annual General) Meeting of the Association was held at the London School of Hygiene and Tropical Medicine on Oct. 29 and 30, 1948. The President, Dr. A. J. Amor, was in the Chair, and seventy-two members attended.

In introducing the Report of the Council for the year 1947–48, Dr. Amor said that four meetings of the Association had been held, three in London and one in Glasgow. The Council had also held four meetings during the year. The outstanding event of the year had been the Ninth International Congress on Industrial Medicine, which had been well supported by members. The Council had replied to the Inter-Departmental Committee on the remuneration of Consultants and Specialists that Industrial Medicine must be regarded as a speciality. The first number of a Quarterly Bulletin had been published, to keep members acquainted with the activities of the Association. The President also reported that the library facilities of the London School of Hygiene and Tropical Medicine had now been made available to members, and it was agreed that Prof. J. M. Mackintosh should be thanked for this gesture. The sub-committee on the provision of medical services for small units had reported earlier in the year and the report was sent to the B.M.A. Occupational Health Committee. In conclusion, the President thanked all members for their whole-hearted co-operation in the working of a successful year.

The Hon. Treasurer, Dr. J. A. A. Mekelburg, then presented the Accounts, which were adopted without discussion. Some discussion then took place on a proposal to increase the annual subscription, but it was decided that the subscription should not be increased for the ensuing year. A proposal to amend the Constitution in relation to Membership was not proceeded with.

The following were elected Officers and Members of the Council for the year 1948–49: *Hon. Secretary:* Dr. J. A. A. Mekelburg; *Hon Treasurer:* Dr. W. G. S. Pepper; *Hon. Editor of Transactions:* Dr. L. Norman; *Council Members (Ordinary Members):* Drs. M. L Dobbie-Bateman, J. S. Spickett, H. F. Chard, W. Gunn, R. E. W. Fisher, L. J. Hayden, N. G. Marr, and S. B. Scott; *Council Member (Associate Member):* Dr. F. Wrigley.

The following were elected to represent the Groups on the Council: Birmingham: Dr. J. G. Billington; Yorkshire: Dr. R. A. Trevethick; London: Dr. G. E. Graves-Peirce; Manchester: Dr. G. Taylor; Nottingham: Dr. J. Magill Young; Scottish: Dr. D. M. Watson; South Wales and West of England: Dr. G. Stenlake-Mundy; and Tees-side: Dr. F. H. C. Beards.

On Saturday morning, Oct. 30, Mr. R. A. Hacking, of Messrs. Richard Thomas and Baldwin, addressed the Association on the subject of the manufacture of steel. Mr. Hacking described the properties of naturally occurring iron and gave an account of the extraction of iron, together with the chemical and physical factors involved in the various processes. The remarkable tenacity of iron for oxygen was shown by the fact that at 600° C. an extremely low vacuum would be required to reduce the metal to the pure element, whereas some other metals, such as silver, could be reduced to the element by heating to this temperature. Chemical reducing processes were the basis of the production of iron, and carbon was used in the process for the production of pig iron, leading to the formation of cast iron, which was the metal run off the bottom of the furnace. Mr. Hacking went on to describe the Bessemer process, in which air is blown through the molten metal to produce steel, and the open-hearth process for the production of steel which was the method most extentively used in Britain today. Over 80 per cent. of steel was produced by the open-hearth process, about 8 per cent. by the Bessemer process, and 4 per cent. by the electric-arc process which was used for the production of high-class steels. Mr. Hacking showed a number of slides to illustrate the details of the various procedures, and went on to describe the geographical distribution of British steel works, which were centred around coal-fields except for the one at Coaby which had been founded in 1935. A section of a furnace capable of producing 600 tons of steel a day was illustrated and described, together with the layout of a dockside steel works in South Wales and that of the very large Hermann Goering plant. At pressures up to 10 lb. per square inch or more, American engineers had succeeded in producing up to 1,700 tons of steel a day from a single furnace; by means of added oxygen it was theoretically possible to increase this to as much as 3,000 tons daily. Mr. Hacking then showed a colour film which his firm had produced to illustrate the details of the various processes concerned in the production of steel. The President, in thanking Mr. Hacking for his most interesting address, said that it was also helpful for Members to see this outline of one of the major industries which would no doubt be one of those visited at the Annual Provincial Meeting in South Wales in 1949.

BIRMINGHAM GROUP

Chairman: Dr. W. Jeaffreson Lloyd,
Guest, Keen, and Nettlefolds Ltd.

Hon. Secretary: Dr. J. G. Billington,
General Electric Co. Ltd., Witton, Birmingham.

A Meeting was held on May 19, 1948, at which the Group discussed the whole question of convalescent homes and rest break and holiday schemes. The Chairman felt that it was not only the so-called working class who required a break, but managements as well.

The first speaker was Mr. Hughes of the Birmingham Hospital Saturday Fund, who said that the Fund's Convaleseent Homes were outside the new Insurance Schemes as no treatment was given, and that they were asking work people to continue their voluntary subscriptions to carry on the homes. (This scheme is now working quite well.) In order to be quite fair to applicants for admission, no person would in future be normally allowed to go to a convalescent home in two consecutive years. Medical Certificates for admission to the homes from industrial medical officers were not accepted, and it was necessary for the patient's own doctors to issue such certificates. The Hospital Saturday Fund sent an average of two hundred people a week to the homes.

Mr. D. M. Gibb (Warden) then spoke of the work done at Windmill House, Weatheroak, Alvechurch, Worcestershire. It was run by the Birmingham Association of Girls' and Mixed Clubs, and during the last five years they had taken some 20,000 people (mostly adolescents) of all kinds and with different backgrounds. The majority wanted to get away from the difficulties of home relationships. He tried to mix convalescents with club members and to accept everyone on the same basis, and also to make people feel they were individuals. The domestic duties were shared, and it was surprising how people talked of their troubles and how confidences were given over the washing-up. In fact, many friendships had been thus made. These troubles could not or would not be spoken of in people's own homes. Mr. Gibb concluded that he would be very pleased for anyone to visit Windmill House at any time, and he felt certain that visitors would not meet sad faces.

Dr. Lloyd spoke warmly of the value of such a home and gave instances of young workers from his factories who had benefited by their stay there and whose whole outlook had been improved.

An outline of convalescent and holiday schemes was then given. Dr. V. V. Brown of Messrs. Rubery Owen Ltd., spoke of the home owned by the firm, which was much appreciated by both men and women. Dr. Brown had the final task of selecting patients. The firm paid the railway fares and there were no charges to the workers. Dr. J. G. Lawson of Messrs. Joseph Lucas Ltd. said that for the past ten years his firm had had a home for women and girls at Weston-super-Mare. This was free to employees, who were selected by a Committee on recommendations by the foreman. Dr. C. H. Hoskyn of the Austin Motor Co. Ltd., said that their workers went to the Hospital Saturday Fund homes and that staff and work-people were helped by two schemes. Dr. J. G. Billington of G.E.C. Ltd. said that this was also so in his firm, who paid the fares to the convalescent homes. Dr. J. A. Duncan of I.C.I. (Metals) Ltd. said that his firm made an allowance for girls selected by the welfare officers. Return fares were paid by the firm.

Dr. J. B. Sherman of Cadbury Brothers Ltd. outlined his firm's comprehensive scheme. There was a men's remedial home at Harleck, owned by the firm, to which persons were sent on recommendation of foremen or shop committee members as being in need of a change either as a result of a strain at work, domestic trouble, or in order to avoid a period of absence from work. Board and travel were paid by the firm, who also gave allowances for children etc. where necessary. There were similar rest break houses for women, who were selected and helped in the same way. In addition the firm makes use of the Hospital Saturday Fund homes for convalescent cases.

Miss Frew (Almoner of the Birmingham United Hospitals) advised all interested to obtain a copy of the Directory of Convalescent Homes issued by the King Edward Hospital Fund, London, at 5*s*. This guide gave the type of cases admitted and whether dressings were done or diets given.

On May 25, 1948, a visit was paid to the Aston Works of Messrs H.P. Sauce Ltd., where members were shown the processes for the making of vinegar, sauces, and pickles. The excellence of the raw materials, the steady improvement in the working conditions, with their emphasis on extreme cleanliness and absence of touch by hand, the efficient laboratory service, and the good "family spirit" shown in the works, were favourably commented upon.

The M.R.C. Unit of the Birmingham Accident Hospital were "at home" to the Group on June 21, 1948, when the Director, Dr. (now Professor) J. R. Squire, had prepared a programme dealing with the control of wound infection and with the problems of occupational dermatitis. There were many demonstrations, including photographs of industrial skin disease, tables showing the composition of normal skin fats, and an ingenious apparatus on the "Archimedean principle" which measured the increase in finger-tip volume in cases of suspected pulp infection. An increase in volume of 17 per cent. or over was an indication for immediate incision. Dr. G. N. Cruickshank showed the effect of various patent and other detergents on the removal of mineral oils from the skin, and showed by means of the ultra-violet lamp how the oil left in or on the skin after washing was readily visible as brilliant fluorescence. This test was convincing to the most sceptical and made us realize how tenacious mineral oils are, especially in the areas of skin where there are many hairs. Dr. G. Ricketts spoke about the natural fats of the skin surface and their relationship to self-sterilization. Dr. J. P. Bull spoke on the importance of minor injuries in causing lost time, and mentioned that Birmingham was especially a centre where fingers were so often injured and where any disability at all rendered the worker relatively useless, as so much of the city's industries demanded fine workmanship from supple fingers. He gave an account of the research work done by the M.R.C. Unit on "Experiments with occlusive dressings of a new plastic" later published (*Lancet*, 1948, **2**, 213). The physical properties, in particular water-vapour permeability, of the nylon-derivative film suitable for wound dressings were described. The film is an effective barrier against micro-organisms, and tested on the human skin, the permeability of this film to water-vapour was shown to be sufficient to prevent the skin from becoming sodden. The bacterial flora of the healthy skin under the occlusive dressing became modified, *Staph. aureus* disappeared, and the variety of organisms was reduced. Clinical trials with the film were stated to be in progress and the preliminary results were promising.

Dr. E. Topley spoke of the work that she and Mr. S. H. Harrison had been doing on systemic penicillin in finger-pulp infection. The investigation was carefully controlled, one group receiving systemic penicillin, the other no general therapy. *Staph. aureus* sensitive to penicillin was isolated from over 90 per cent. of operation swabs. Systemic penicillin effectively reduced the incidence of positive swabs at subsequent dressings. Clinically the healing time was shorter in the penicillin series (average, controls 20·0, penicillin 14·7 days), and there was a lower complication rate. Operation was delayed in a series of patients on systemic penicillin. With delay fewer were incised, but the unsatisfactory

results in the incised patients made this delay undesirable in routine treatment. Evidence was shown that local penicillin at operation and systemic penicillin for a complication are both much less effective than systemic penicillin started before operation. The average healing times improved throughout the investigation (for example, first months 35·3 days, last months 15·6 days). Evidence was given to suggest that one cause for the improvement was the use of a minimal incision in place of the classical hockey-stick incision.

On Nov. 9, 1948, Mr. Colin Johnston, who for the past three years has been conducting otological clinics in a number of large Birmingham factories gave a report of his work on infective ear disease. This paper has since been published (*Brit. med. J.*, 1948, **2**, 1049). Chronic ear diseases, in particular chronic suppurative otitis media, are potent causes of inefficiency and invalidism. A random selection of 1,902 employees showed 3·3 per cent. suffering with suppuration in the middle ear and 17·8 per cent. with active or healed middle-ear disease. A total of 1,711 patients complaining of ear, nose, or throat symptoms were examined at factory clinics; 389 were found to suffer from disease of the pinna and external auditory meatus and 274 from C.S.O.M. Daily treatment after efficient diagnosis was essential, and of a hundred patients so treated thirty-eight might expect to have a dry ear after 5·2 weeks and to keep it dry for at least six months, 45 would have a dry ear but would relapse in less than six months, although standing a good chance with subsequent treatment, six would be rendered quiescent, and eleven would need a surgical operation. The results showed that conservative treatment would clear up infection in a high proportion of cases, but the prospects of obtaining a lifelong cure were poor. It was found that in manual workers productive efficiency was affected more by pain than by deafness, but that the latter might be a handicap to promotion. It was considered that the future expansion of otological treatment in factory medical departments was feasible and would reduce the present overloading of the hospital services.

YORKSHIRE GROUP

Chairman: Dr. S. A. Underwood,
Rowntree and Co. Ltd., The Cocoa Works, York.

Hon. Secretary: Dr. C. Cresdee,
I.C.I. (Dyestuffs Division), Huddersfield.

A meeting of the Group was held at the Algernon Firth Institute of Pathology on Oct. 2, 1948. Drs. Underwood and Cresdee were elected Chairman and Hon. Secretary for the year 1948–49. Dr. Trevethick was elected Group Representative to the Council.

It was decided to change the name of the Group from the Leeds Group to the Yorkshire Group.

A discussion took place about methods necessary for stimulating the activities of the Group. It was realized that with a scattered membership it was difficult for members to attend ordinary meetings. The Chairman and Secretary thought the spreading of the places of meetings might help, and the Chairman suggested that four meetings should be held during the winter—two in Leeds, one in Sheffield, and one in York—and that the meetings should consist of a general discussion of the problems of members in relation to their own particular industry, and that one of the medical officers of the area in which the meeting was held should review his own particular industry and its problems.

A meeting was held in Sheffield on Saturday, Dec. 4, 1948. In the morning a tour was made of the Works of Steel, Perch, and Tozer. The Works Medical Officer, Dr. Trevethick, acted as guide. Instructive hours were spent in following the processes of manufacture from the first stages of the furnaces to the finished product of extruded steel and steel strips. The details of each section, the accompanying hazards, and the medical problems arising therefrom, were explained by Dr. Trevethick. During the past eleven months the steel output from this particular works reached the record of over three-quarters of a million tons. The tour ended with a visit to the medical department, where cases of skin grafting, burns, and other skin conditions were shown.

In the afternoon, twelve members were present at the ordinary meeting. Dr. Hartley, of Samuel Fox and Co. Ltd., addressed the meeting on the medical aspects of the steel industry. He pointed out that in many cases the buildings had been in use for some sixty to a hundred years, and conditions had remained the same except in modern works now being erected. On the credit side, however, there were extremely good labour relations. In his particular firm there had been no industrial dispute for a hundred years, and there had been no major upset in the steel industry for over forty years. The wages were high in comparison with many other industries. From the hazard point of view, accidents took first place, and as the medical service in the steel industry was still comparatively young a start was made by establishing an efficient accident service. The frequency rate of accidents was not disproportionately high, although the lighter side of the industry had many more minor accidents than the heavy side, where if an accident occurred it was usually severe. In 1947 in his particular works there were five fatal accidents and five with a permanent partial disability. Dr. Hartley analysed the accident attendances over a period, and bruises, cuts, burns, and foreign bodies in the eye represented the major incidence. There were few toxic risks encountered, though the recent introduction of lead shot which had been incorporated into the steel was something to be watched very carefully. Dermatitis was generally due to oil and grease or to wear and tear. Investigation was beginning into the question of whether steel workers were prone to respiratory troubles or cancer. They worked in a very hot and dusty environment.

Dr. Trevethick then emphasized the fact that very extensive alteration to the present plant would be needed to improve local working conditions in the steel industry. In the early stages of his appointment as Works Medical Officer Dr. Trevethick had spent most of his time in becoming familiar with the works and getting to know the workers. The future would be along the lines of preventative medicine, and he instanced again the use of lead and other toxic materials that might be used in the manufacture of steel. So far, there had been no apparent ill effects. Dr. Trevethick mentioned the " wear and tear " dermatitis which was a very real problem and occurred after many years. The people in the spring-making department were exposed to multiple small burns. Heat stroke was another condition which had caused some anxiety, but it was now much reduced as a result of the provision of salt in tablet form, which the men preferred to saline drinks. Whereas, previous to the introduction of the sugar-coated saline tablets, workers complained that they were weary by evening, they now said they were less tired at the end of the working day. Sepsis was

not an uncommon condition, and resulted from the many minor burns and scratches that were a hazard of the work.

Dr. Watson of Newton, Chambers and Co. Ltd., then addressed the members. His industry was mainly associated with iron foundries and chemical works. He demonstrated many interesting and practical methods of dealing with injured fingers and toes. He thought a good cosmetic result went with a good functional ability. Dr. Watson showed photographs and *x* rays of injured digits.

A discussion followed, and Dr. Trevethick was thanked for the instructive day.

SOUTH WALES AND WEST OF ENGLAND GROUP

Chairman : Dr. J. S. Spickett,
Richard Thomas and Baldwins Ltd.,
Bridgend, Glamorganshire.

Hon. Secretary : Dr. G. Stenlake-Mundy,
The Bristol Aeroplane Company,
Filton House, Bristol.

On Sept. 30, 1948, members of the Group visited the Royal Ordnance Factory at Pembrey. After an excellent lunch presided over by Mr. R. O. Bishop, Superintendent of the factory, a visit was made to the portion manufacturing ammonium nitrate. The plant devoted to the extraction of phosphorus from bombs and shells was also visited, and particular reference was made to precautions necessary for carrying out this work. The following departments were also included in the itinerary: the factory library, canteen and changing rooms, laundry, and boot repairing shop. The last three departments were really part of the extensive safety measures carried out in this factory, there being changing rooms, laundries for clothes, individual showers, baths, cubicles lined with white tiles, and drying rooms for damp clothes. Every worker was given each week a suit of special clothes; and special boots in certain parts of the factory.

A clinical meeting was held on Oct. 23, 1948, at the dermatological department of the Cardiff Royal Infirmary by kind invitation of Dr. Hodgson.

On Dec. 1, a visit was paid to the works of the Bristol Aeroplane Company Limited at Filton. Members visited the kitchens and dining halls. Bristol Wayfarers and Freighters were seen in course of construction. In the "press shop" special note was taken of the guarding of both large and small presses. The large Brabazon Hangars and the Brabazon I were inspected; then the various processes in the Rodney Works plating shop were seen and discussed. A foundry treating high-grade steel used in jet engines was seen, and also the engine test houses.

TEES-SIDE GROUP

Chairman : Dr. H. Fellows,
Dorman Long and Co., Ltd., Middlesbrough.

Hon. Secretary : Dr. J. B. Adamson,
Ministry of Fuel and Power,
Newcastle-upon-Tyne.

A meeting was held at Durham on Nov. 10, 1948, when Prof. Alexander Kennedy of the Department of Psychological Medicine, Royal Victoria Infirmary, Newcastle-upon-Tyne, spoke on psychological medicine and its relation to industry. He said it was essential for the works medical officer to have a general working knowledge of psychiatric methods, and towards this end teaching courses were to be established. Prof. Kennedy included observations on rehabilitation, compensation, and the organization of a mental health service in the region.

A meeting was held at Billingham on Dec. 15, 1948, when Dr. W. Gillies Annan, Medical Referee (Dermatologist) Durham County, and North Yorkshire, described the salient features and methods of treatment of fourteen different skin diseases.

LONDON GROUP

Chairman : Dr. G. E. Graves Peirce,
Railway Executive, London Midland Region,
Euston Station, London.

Hon. Secretary : Dr. R. E. W. Fisher,
Chief Medical Officer,
South Metropolitan Gas Co., London.

A meeting of the London Group was held at the London School of Hygiene and Tropical Medicine on Nov. 11, 1948. Dr. Graves Peirce was in the Chair and Mr. J. H. Simpson delivered an address on the deaf workman. Mr. Simpson dealt mainly with the problem of the workman who becomes deaf after he has taken up employment. He dealt with the various causes of deafness and explained how they could be prevented and also how early cases of deafness could be detected. After Mr. Simpson's address a representative of a commercial firm demonstrated an audiometer.

On Dec. 16, a meeting of the Group was held at Pimm's Restaurant. Mr. H. H. Kenshole read a paper entitled "Fringes of History," dealing with ailments of various historical personages and how they affected the course of history.

SCOTTISH GROUP

Chairman : Dr. D. Gordon Robertson,
Imperial Chemical Industries Ltd.,
Nobel Division, Stevenston, Ayrshire.

Hon. Secretary : Dr. William Hunter,
Wm. Collins Sons and Co. Ltd., Glasgow.

On April 14, 1948, the Scottish Group visited the Royal Infirmary, Glasgow, where Prof. L. J. Davies opened a discussion on hæmatology and industrial medicine.

During the week beginning June 14, the Scottish Group entertained the Association in Glasgow; the Proceedings of this meeting were reported in the January 1949 issue of the Journal.

A business meeting was held on Nov. 17, and an address was given by Dr. G. G. Browning, Consultant to the Ministry of Labour. Dr. Browning dealt with industrial rehabilitation from the aspect of the Ministry, and described in detail the facilities available for retraining, and the problems associated with this service. Considerable discussion followed.

On Dec. 11, the Group held a Social Meeting.